Identification and Care of Patients at Risk of Post-Stroke Dementia

Thesis submitted for the degree of Doctor of Philosophy

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Abstract

Stroke can directly cause cognitive difficulties but also increases the risk of future dementia. There is often less focus on these consequences during standard care, which tends to concentrate on physical function. The seven publications described in this thesis focussed on four aims, which were to: a) describe the impact of cognitive difficulties post-stroke over time b) understand patient and professional views regarding current care for stroke-survivors with memory problems c) describe the acceptability and accuracy of dementia risk prediction models following stroke d) understand healthcare professional views about how to meet the cognitive needs of stroke-survivors. A mixed-methods approach was used to address these aims including: a) A systematic review of studies found there was a tendency towards cognitive decline, but this was not consistent as patients post-stroke can stabilise or even recover; b) Semi-structured interviews with i) stroke-survivors reporting memory difficulties and their family carers and ii) primary and secondary care professionals consistently reported clear gaps in care for stroke survivors with memory deficits; c) Harmonisation of international stroke cohorts to externally validate existing dementia risk prediction models which have not validated well in stroke populations. Further, in the qualitative interviews, patients, family carers and healthcare professionals identified challenges to their implementation; d) A national electronic-Delphi survey found that stroke clinicians believe assessment of post-stroke cognition needs better integration into services with clarification of when and where this should be done to streamline access. The gaps in current services mean that the support available to care for and identify those at greatest risk for dementia is lacking. Patients and carers should be offered information about the long-term cognitive consequences post-stroke. If required, they should be encouraged to seek assistance in the community with the aim of being directly referred back into specialist services for assessment and intervention.

Dedication

To Michelle, Tristan and Alana

Acknowledgements

The work presented here would not have been possible without the help, support, collaboration and generosity of a number of individuals. In particular I wanted to firstly thank my academic supervisors: Professor Louise Robinson, Professor Catherine Exley, Professor. Christopher Price and Professor Blossom Stephan. They have seen the highs and lows over the last six years. I thank them for their support, patience, friendship and mentorship during the time it took from preparing to submit a bid for this NIHR Doctoral Research Fellowship to completion of this thesis in testing times. They have individually contributed significantly to my personal development as I've learnt to navigate this clinical academic role whilst also learning the ropes of parenthood. They have had on many occasions dig me out of what we have termed my "wormhole" moments, which I am always grateful for.

I would also like to thank my co-authors on the papers presented here for their time and expert guidance in preparing these papers. I would also like to thank my annual assessors Professors Gill Rowland and Joy Adamson, Dr. Richard Lee and in particular Professor Carol Jagger who has been there from the beginning. I would also like to thank my funder NIHR for seeing the potential in this area and for supporting me with a Doctoral Research Fellowship.

Most importantly I'd like to thank the wonderful participants who gave up their time, invited me to their homes and remained enthusiastic about the project throughout the process. My hope has always been that I would be able to share their stories with the wider public and scientific community so their voices could be heard. In line with this, my sincerest of thanks to my participant advisory panel who have been with me throughout my PhD. The annual feedback meetings were always amongst my highlights. It was always a pleasure to work alongside them, to share our stories and experiences with one another. They taught me the value of patient and public participation in the research process and I hope that they can continue to be enthused by research and ably assist others as they have done with me.

My sincerest thanks to my academic GP colleagues, in particular Drs Johanne Dow, Lisa Newton and Robert Barker. We have traversed the challenges of academic primary care together. Learning how to be better GPs whilst also learning how to be better researchers has been challenging. But their support, advice and humour has what has always been what has helped me overcome the disappointments and difficult times.

A special thanks go to family. To my parents for teaching me the importance of hard work and perseverance. To my siblings for their invaluable feedback to me both at the start and at the end of the process. To my children Tristan and Alana, who have patiently waited for me to finish my work (most of the time) and for always putting a smile on my face. Finally, and most importantly, my thanks to my wife Michelle. She may not have always understood what it was that I was doing but without her love, encouragement, unfaltering support and patience this piece of work would not have been completed. I thank her for always putting the family first and making sure we were all well looked after even when I would time away on my many visits abroad!

Declaration

I declare that this thesis is my own work and that I have correctly acknowledged the work of others. This submission is in accordance with University and School guidance on good academic conduct

I certify that no part of the material offered has been previously submitted by me for a degree or other qualification in this or any other University

I confirm that the word length is within the prescribed range as advised by my school and faculty

I confirm that this thesis contains collaborative work and my independent contributions have been outlined in the appropriate co-authorship forms found in this thesis.

Signature:

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Contents

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Deleted: 21

List of Table(s)

List of Figure(s)

Abbreviations

AD	Alzheimer's Disease
ADDTC	State of California Alzheimer's Disease Diagnostic and Treatment Centers
ANU-ADRI	Australian National University AD Risk index
AUC	Area under the curve
CAIDE	Cardiovascular Risk Factors, Aging and Dementia
CASP	Cognitive Assessment Scale for Stroke Patients
CI	Confidence Interval
COSMIC	Cohort Studies of Memory in an International Consortium
CQUIN	Commissioning for Quality and Innovation
DeNDRoN	Dementias and Neurodegenerative Diseases Primary Care Clinical Studies
FINGER	Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability
GP	General Practitioner
LIBRA	Lifestyle for Brain Health
MMSE	Mini-Mental State Examination
MoCA	Montreal Cognitive Assessment
NCD	Neurocognitive Disorder
NICE	National Institute for Health and Care Excellence
NINDS-AIREN	National Institute of Neurological Disorders and Stroke – Association Internationale pour la Recherché et l'Enseignement en Neurosciences
NSC	National Screening Committee
OCS	Oxford Cognitive Screen
PPI	Patient and public involvement

preDIVA	the Prevention of Dementia by Intensive Vascular care
PSD	Post-stroke dementia
RDS	Research Design Service
RR	Risk Ratio
SSNAP	Sentinel Stroke National Audit Programme
TIA	Transient Ischaemic Attack
UK	United Kingdom
VaD	Vascular Dementia
VCI	Vascular Cognitive Impairment
VMCI	Vascular Mild Cognitive Impairment

Patient and Public Involvement

Patient and public involvement (PPI) has helped shape the thesis since the beginning. As part of the process in obtaining my doctoral fellowship, I felt it was important that what I was proposing was appropriate, acceptable and important to people who are affected by stroke and dementia. The first draft of my research proposal focused on developing the use of risk prediction models only. It was initially reviewed positively by VOICENorth (a dedicated PPI organisation to involve the public on ageing research). Three participants also expressed an interest in being part of the programme. The same research proposal was presented to the Dementias and Neurodegenerative Diseases Primary Care Clinical Studies (DeNDRoN) group. This consisted of both clinical and non-clinical staff as well as patients with either dementia or other neurodegenerative diseases. This group helped to prioritise the research objectives of the proposal and identify a clinical context, where the risk prediction models being validated would be particularly useful. The views of the patients led to the establishment of a further phase in the study, which they felt had been lacking in the original proposal. The current work was presented to two further groups: a lay membership consumer's panel on behalf of the research design service (RDS) and the North East Stroke Research Patient and Carer Panel. There was general consensus from the RDS panel that the proposal would provide significant benefit not only in terms of identifying at risk individuals but also for information provision to the general public through dissemination of findings. They commented that incorporating views of stroke patients and their carers as part of the PPI process and a research management group would strengthen the study. The programme of work was extremely well received by the 12-member panel from the North East Stroke Research Patient and Carer Panel with panel members offering to be part of the participant advisory group and also take part in one of the phases. The finalised proposal was sent to our local DeNDRoN PPI panel where reviewers identified this project as an important piece of work and one in which a lay audience could understand the intended benefits. Throughout the PhD itself I have also had a participant advisory group who met at least annually to review the work and provide advice with regards to e.g. dissemination.

Outputs during PhD Registration

The following published papers make up my thesis submitted for the degree of Doctor of Philosophy:

Published Papers (PP)

PP1. Tang EYH, Amiesimaka O, Harrison S, Green E, Price C, Robinson L, Siervo M, Stephan B. **Longitudinal Effect of Stroke on Cognition: A Systematic Review.** Journal of the American Heart Association (2017): 7(2). pii: e006443

PP2. Tang EYH, Price C, Stephan B, Robinson L. Exley C. **Impact of Memory Problems Post-Stroke on Patients and their Family Carers: A Qualitative Study.** Frontiers in Medicine (2020); 7; 267

PP3. Tang EYH, Price C, Stephan B, Robinson L, Exley C. **Gaps in Care for Post-Stroke Patients Reporting Memory Deficits: Views of Healthcare Providers.** BMC Health Services Research (2017); 17 (1):634

PP4. Tang EYH, Price C, Stephan BCM, Robinson L, Exley C. **Post-Stroke Memory Deficits and Barriers to Seeking Help: Views of Patients and Carers.** Family Practice (2019); 36(4):506-510

PP5. Tang EYH, Price CI, Robinson L, Exley C, Desmond D, Kohler S, Staals J, Lam B, Wong A, Mok V, Bordet R, Bordet A-M, Dondaine T, Lo JW, Sachdev P, Stephan B, STROKOG Collaboration **Assessing the Predictive Validity of Simple Dementia Risk Models in Harmonised Stroke Cohorts.** (Stroke, 2020); 51 (7); 2095 -2102

PP6. Tang EYH, Exley C, Price C, Stephan B, Robinson L. **The Views of Public and Professional Stakeholders on Risk Assessment Tools for Post-Stroke Dementia: A Qualitative Study.** BMJ Open (2019)**;** 9(3):e025586

PP7 Tang EYH, Robinson L, Exley C, Flynn D, Stephan BCM, Price C. **Care Priorities for Stroke Patients Developing Cognitive Difficulties: A Delphi**

Survey of UK Professional Views. BMC Health Services Research (2020); 20(1); 717

Oral Presentations

1. Tang EYH, Harrison S, Green E, Price C, Stephan B. **The Longitudinal Effect of Stroke on Cognition.** Oral presentation at WONCA Europe (Copenhagen, 2016)
2. Tang EYH, Price CM, Stephan BCM, Robinson L, Exley C. **Barriers to Timely Diagnosis of Post-Stroke Dementia: Views of Patients and Carers.** Oral Presentation at SAPC North (Kendal, 2017)
3. Tang EYH. **Identification and Care of Patients at Risk of Post-Stroke Dementia.** Stroke Research Team Meeting (4th July 2018), University of Central Lancashire
4. Tang EYH. **Care of Stroke-Survivors at Risk of Dementia in the UK.** Invited speaker (13th November 2018), University of Hong Kong
5. Tang EYH, STROKOG Consortium. **External Validation of Dementia Risk Scores in Stroke Cohorts.** Invited speaker for STROKOG Symposium (16th November 2018), VASCOG (Hong Kong, 2018).
6. Tang EYH. **Predicting Dementia After Stroke.** Invited speaker for UK Stroke Forum (6th December 2018), UK Stroke Forum (Telford, 2018)
7. EYH Tang, D Flynn, L Robinson, C Exley, B Stephan, C Price. **Prioritising Actions for the Six-Month Review for Post-Stroke Survivors Presenting with Cognitive Impairment: A Delphi Study.** Oral Presentation, OPSYRIS (Oxford, 2019)

Poster Presentations

1. Tang EYH, Price C, Exley C, Stephan B, Robinson AL. **Identification of Post-Stroke Cognitive Impairment in the UK.** E-poster presentation at WONCA Europe (Copenhagen, 2016)
2. Tang EYH **External Validation of Risk Prediction Tools for Dementia in Stroke Populations.** Flash presentation at ARUK Early Careers Day 2019 (Harrogate)
3. Tang EYH, Robinson L, Exley C, Price C, Chen C, Allan L, Köhler S, Mok V, Bordet R, Desmond D, Sachdev P, Lo J, STROKOG Consortium, Stephan B.

External Validation of Risk Prediction Tools for Dementia in Stroke Populations. Poster presentation at ARUK 2019 (Harrogate)

Other Notable Outputs

Non-Thesis Publications

1. Tang EYH, Harrison S, Errington L, Gordon M, Visser PJ, Launer L, Novak G, Dufouil C, Siervo M, Robinson AL, Stephan BCM, **Current Developments in Dementia Risk Prediction Modelling: An Updated Systematic Review** PLoS One (2015) Sep 3;10(9):e0136181. doi: 10.1371/journal.pone.0136181. eCollection 2015.
2. Tang EYH, Harrison SL, Albanese E, Gorman TJ, Rutjes AWS, Siervo M, Stephan B., **Dietary interventions for prevention of dementia in people with mild cognitive impairment** Cochrane Database of Systematic Reviews, Article first published online: 9 October 2015, **DOI:** 10.1002/14651858.CD011909
3. Siervo M, Lara J, Munro A, Tang EYH, Rutjes AWS, Stephan B, **Dietary interventions for maintaining cognitive function in cognitively healthy people in late life** Cochrane Database of Systematic Reviews, Article first published online: 9 October 2015, **DOI:** 10.1002/14651858.CD011910
4. Tang EYH, Burn, D, Taylor JP, Robinson, AL., **Dementia with Lewy Bodies: The Emerging Role of Primary Care**, European Journal of General Practice (2015) 22(1); 53 - 57
5. Tang EYH, Fox H, Gajria C, Welsh V, Mehrotra, A**, Development of an Audit Toolkit for Use in Resource-Poor Countries,** Education for Primary Care (2016), 27 (1), 79-80
6. Stephan BCM, Tang EYH, Muniz-Terra G, **Composite Risk Scores for Predicting Dementia** Current Opinion in Psychiatry (2016), 29 (2); 174-80
7. Fox H, Tang E, **Family Doctors' Knowledge of and Attitude Towards Migrant Access to Healthcare Across Europe and Beyond.** British Journal of General Practice (2016). Jun;66(647):313. doi: 10.3399/bjgp16X685405
8. Tang EYH, Fox H, Gajria C, Modi R. **Challenges Facing Early Career Primary Care Researchers Across Europe.** Education for Primary Care (2016) May 13: 1 – 2
9. Fowkes R, Byrne M, Sinclair H, Tang E, Kunadian V, **Increased Risk of Coronary Artery Disease among Patients with Dementia and the**

Potential Mechanisms Linking the Two Conditions: a Review, CAD (2016) 27 (6); 511 - 20

10. Tang EYH, Birdi R, Robinson AL, **Attitudes to Diagnosis and Management in Dementia Care: Views of Future General Practitioners,** International Psychogeriatrics (2016) 9:1 – 6
11. Harrison SL, Tang EYH, Keage H, Taylor JP, Allan L, Robinson L, Jagger C, Rockwood K, Stephan BCM. **A systematic review of the definitions of Vascular Cognitive Impairment-No Dementia (VCI-ND) in cohort studies.** Dementia and Geriatric Cognitive Disorders (2016); 42(1-2): 69 – 79
12. Petrazzuoli F, Vinker S, Koskela TH, Frese T, Buono N, Soler JK, Ahrensberg J, Asenova R, Boreu QF, Peker GC, Collins C, Hanževački M, Hoffmann K, Iftode C, Kurpas D, Reste JYL, Lichtwarck B, Petek D, Pinto D, Schrans D, Streit S, Tang EYH, Tatsioni A, Torzsa P, Unalan PC, van Marwijk H, Thulesius H. **Exploring dementia management attitudes in primary care: a key informant survey in 25 European and Mediterranean countries**. International Psychogeriatrics (2017) Sep;29(9):1413-1423. doi: 10.1017/S1041610217000552.
13. Bridgwood B, Willoughby H, Attridge M, Tang EYH, **The Value of Exchange Programs for Early Career Family Doctors**, Education for Primary Care (2017); 28(4); 232 – 236
14. Tang EYH, Robinson L, Stephan BCM. **Risk Prediction Models for Post-Stroke Dementia**. Geriatrics (2017); 2(3), 19.
15. Tang EYH, Robinson L, Stephan BCM. **Dementia Risk Assessment Tools: An Update.** Neurodegenerative Disease Management
16. Modi R, Chapman L, Gajria C, Tang E. **'The Best Laid Plans of Mice and Men': A Workshop to Teach the Application of Evidence Based Medicine (EBM) in Low- and Middle-Income Countries (LMICs).** Education for Primary Care (2017); 29(2):107-112. doi: 10.1080/14739879.2017.1413597.
17. Bridgwood B, Park J, Hawcroft C, Kay N, Tang EYH. **International Exchanges in primary Care – Learning from thy Neighbour.** Family Practice (2018); 35(3):247-252. doi: 10.1093/fampra/cmx101.
18. Stephan BCM, Birdi R, Tang EY, Cosco TD, Donini LM, Licher S, Ikram MA, Siervo M, Robinson L. **Trends in Dementia Prevalence and Incidence Worldwide: A Systematic Review.** Journal of Alzheimer's Disease (2018); 66(2):653-680. doi: 10.3233/JAD-180375

19. Sahota K, Goeres P, Kelly M, Tang EYH, Hofmeister M, Alberti H. **Intellectual Stimulation in Family Medicine, a Qualitative Study of Student Perceptions in Canada and the UK.** BJGP Open (2020)

Non-Thesis Oral and Poster Presentations

1. Fox H, Tang EYH. **Knowledge of and Attitudes Towards Migrant Healthcare Across Europe and Beyond.** Oral presentation at WONCA Europe (Copenhagen, 2016)
4. Tang EYH, Welsh V, Whalley K, Willoughby H, Bridgwood. **Expectations and Experiences of UK Family Doctors Prior to European Exchange Placements.** Oral presentation at WONCA Europe (Copenhagen, 2016)
5. Tang EYH, Birdi R, Robinson AL. **Management of Dementia in the UK: Views of Future General Practitioners**. Invited speaker at Dementia symposium at WONCA Europe (Turkey, 2015)
6. Tang EYH, Fox H, Modi R, Gajria C. **Integrating a Research Career into Practice.** Workshop at WONCA Europe (Turkey, 2015)
7. Tang EYH, Fox H, Modi R, Cajria C. **An evidence based approach – a help or hindrance for GPs working abroad?.** Workshop at WONCA Europe (Copenhagen, 2016)
8. Tang EYH **Towards Better Post-Diagnostic Care of Dementia in Europe**. Speaker and symposium lead at WONCA Europe (Copenhagen, 2016)
9. Tang EYH, Creavin S, Robinson AL. **Towards Better Care of Dementia in the Community** Workshop at RCGP (Harrogate, 2016)
10. Willoughby H, Mir S, Shah D, Modi R, Whalley K, Tang EYH. **The Impact of Observing General Practice in Europe through the Hippokrates Exchange Program: A Qualitative Study.** Poster presentation at the RCGP Annual Conference (Glasgow, 2015)
11. Mehrotra A, Fox H, Gajria C, Welsh V, Prynn J, Tang EYH. **The Development of an Audit Toolkit for Use in Resource Poor Settings**. Poster presentation at the RCGP Annual Conference (Glasgow, 2015)
12. Fox H, Mir S, Ramsay R, Thorne J, Kavasogullari C, Chetty U, Shah D, Mehrotra A, Clark E, Modi R, Whalley K, Shonpal R, Stappels N, Oblensky L, Bridgwood B, Gajria C, Tang EYH. **Impact and Achievements of the RCGP**

Junior International Committee. Poster presentation at the RCGP Annual Conference (Glasgow, 2015)

13. Tang EYH, Birdi R, Robinson AL. **Knowledge and Attitudes of Future General Practitioners in Dementia Care**. Poster presentation at the RCGP Annual Conference (Glasgow, 2015)
14. Tang EYH, Fox H. **The Experiences and Attitudes Toward International Primary Care Amongst Family Doctors Across Europe.** Poster presentation at WONCA Europe (Copenhagen, 2016)
15. Tang EYH, Bridgwood B, Park J, Hawcroft C, Kay N. **The Benefits and Challenges of Primary Care Exchanges: A Systematic Review.** Poster presentation at RCGP Annual Conference (Harrogate, 2016) – Best Poster Prize (International)
16. Modi RN, Gajria C, Tang EYH, "**The Best Laid Plans of Mice and Men" Applying Evidence-Based Medicine (EBM) in Low- and Middle-Income Countries (LMICs).** Poster presentation at WONCA 2017 (Prague)
17. Sahota K, Alberti, Tang E. **"Medical Student Perceptions of General Practice as an Intellectually Stimulating Career"**. Poster presentation at SAPC North 2018 (Kendal)
18. Sahota K, Goeres P, Hofmesiter M, Kelly M, Tang E, Alberti H. **Just coughs and colds? Student perceptions of intellectual stimulation in General Practice.** Poster presentation at ASME 2019 (Glasgow)
19. Goeres P, Sahota K, Hofmesiter M, Tang E, Alberti H, Kelly M. **Just Coughs and Colds. Medical student perceptions of intellectual stimulation and academia in family medicine**. Oral presentation (Family Medicine Summit, 2019)
20. Kelly M, Tang E, Goeres P, Alberti H. **Intellectual Stimulation in Family Medicine, A Qualitative Study of Student Perceptions in Canada and the UK.** Oral presentation (NAPCRG, 2019)

Miscellaneous

2016	WONCA Europe 2016 (Copenhagen) Scholarship (1000 Euros)
2016	Best Poster Prize (International) (RCGP 2016, Harrogate)
2016	#ThinkGP Ambassador (Academic GP), *Royal College of General Practitioners*

2017	Junior Research Award (grand winner), The Vasco da Gama Movement
2017 – present	Appointment as a NIHR CRN GP Engagement lead and GP Champion
2018 – 2019	Appointment as the RCGP North East Faculty's First5 Lead
2020 – present	DEMON Network, National Clinical Lead

Chapter 1: Why is post-stroke dementia a problem?

1.1 Background and Rationale

Cerebrovascular disease is a common cause of dementia in old age with stroke being the second most common cause of acquired cognitive impairment and dementia (O'Brien et al., 2003). Although dementia is frequent after stroke, and can include different dementia subtypes e.g. vascular dementia and Alzheimer's disease (Desmond et al., 2000), not all stroke-survivors who develop cognitive problems meet the criteria for dementia (Sun et al., 2014). Cognitive impairment following a stroke is associated with institutionalisation, disability and increased mortality (Leys et al., 2005b). Further, cognitive impairment post-stroke also leads to poorer quality of life (Ankolekar et al., 2014). For some, cognitive impairment may progress to a dementia illness. With an ageing population and a decline in mortality after stroke (Rothwell et al., 2004), the rates of post-stroke dementia will increase particularly since the incidence of stroke (Rothwell et al., 2005) and dementia (Fratiglioni et al., 2000) both rise exponentially with age. Despite this, cognitive impairment, which may be as common as other neurological (motor and sensory) deficits, is an often-overlooked and neglected consequence post-stroke (Jacova et al., 2012).

The levels of early cognitive impairment post-stroke is concerning with over half of stroke-survivors found to have cognitive impairment after 6 months in one study (Mellon et al., 2015). Looking beyond 6 months, in the UK, long-term cognitive impairment exists even in 22% and 21% of patients at 5 and 14 years respectively post-stroke (Douiri et al., 2013). Pooled dementia rates in hospitalised stroke survivors indicate that 10% have dementia within the first year after their first-ever stroke (Pendlebury and Rothwell, 2009, Pendlebury, 2012). This increases to over 30% in those with recurrent stroke (Pendlebury, 2012, Pendlebury and Rothwell, 2009). However, it is not clear what happens to stroke survivors beyond this early post-stroke period. Stroke-survivors' cognition may remain stable, improve over time or progress to dementia following their stroke (Rasquin et al., 2005, Ballard et al., 2003). Aetiologically, it is likely that factors including large and small vessel disease as well as neurodegenerative pathology combine to determine the pattern of cognitive deficit in the post-stroke individual (Kalaria et al., 2016). Indeed, cognitive deficit is prevalent in the majority stroke survivors even with successful clinical recovery (Jacova et al., 2012).

Stroke care has been identified as a clinical priority by the NHS Long Term Plan, with one of the aims to improve post-hospital rehabilitation (National Health Service, 2019). The Intercollegiate Stroke Working Party has produced expert consensus guidance for clinical services (Intercollegiate Stroke Working Party, 2016). In the 5th edition, a recommendation (2.12.1F) for stroke services is that it should "include clinical neuropsychology/clinical psychology provision for severe or persistent symptoms of emotional disturbance, mood or cognition." including routine follow-up after hospital discharge and annually thereafter (Intercollegiate Stroke Working Party, 2016). By providing these reviews, it is hoped that stroke-survivors can feel supported in the long-term and provide access to other specialist services, even though these are not well defined. This had led to the implementation of the six month reviews for stroke survivors by the Commissioning for Quality and Innovation (CQUIN) (NHS England, 2019). It is clear however that stroke survivors continue to feel unsupported. A survey by the Stroke Association found that 77% of stroke survivors have problems with their memory and nearly 50% said that the support they received for memory and fatigue problems was poor (Stroke Association, 2016). Research into cognition is important to stroke-survivors, caregivers and health professionals (Pollock et al., 2014). In contrast, physical recovery is well researched with evidence showing improvements following organised rehabilitation with personal goal setting (Van Peppen et al., 2004).

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Given that a proportion of individuals may go onto develop dementia, earlier identification of those at-risk particularly for a future dementia illness could be one way to ensure patients are provided with the support, services and interventions they need to continue to live well in the community. One approach in clinical services, which has also been well researched in dementia, is the concept of risk assessment or prediction. Numerous models have actually been developed to predict an individual's risk of future dementia for the general population (Hou et al., 2019, Stephan et al., 2010, Tang et al., 2015). There has been one model developed for stroke patients (Lin et al., 2003). However, none are currently being used clinically due to a lack of assessment in terms of transportability, generalisability and also acceptability to patients and health professionals.

1.2 Problems Identified

Despite the frequency of post-stroke cognitive impairment and dementia, it is not clear what happens clinically. This can result in the patients themselves

expressing dissatisfaction with current clinical services. Although acute stroke is managed in secondary care, primary care will inevitably take over the management of these individuals. However, there is no national consensus around the role of each team in the care of stroke-survivors with cognitive difficulties. If risk prediction models were to be used in the context of stroke, then we need to assess whether existing models are sufficient for stroke-survivors to predict dementia or whether further development work is needed. It is also important to consider where these models sit in the clinical care pathway.

1.3 Thesis Overview

1.3.1 Research question(s):

Are current clinical services able to identify and support stroke-survivors at risk of post-stroke cognitive difficulties and dementia?

1.3.2 Aims and Objectives

The aim of this programme of work was to critically review the care received by people who have had a stroke and are therefore at increased risk of dementia. Several broad aims were set in the hope of answering this through the different phases of work planned:

i) To describe the impact of cognitive difficulties post-stroke over time
ii) To describe the current care provision from the perspectives of patients, carers and key professionals
iii) To explore the use of risk prediction tools to identify those most at risk and
iv) To seek the views of professionals on the key findings from objectives (i) and (ii) with a view to suggesting improvements in future care.

1.3.3 Supporting Chapters and Papers

To support this thesis, there are seven published papers.

Chapter One aims to provide an introduction to the thesis and why this body of work is necessary.

Chapter Two is a literature review around the epidemiology and scale of the problem and presents the reasons for better care of this stroke population and challenges that healthcare services currently face.

Chapter Three synthesises the available data, in the form of a systematic review, around the longitudinal trajectory of cognitive test scores in stroke over time. This chapter includes: **PP1:** (Tang et al., 2018a).

Chapter Four presents qualitative research conducted with stroke-survivors and their family carers with particular emphasis on the impact on their daily lives. This chapter includes **PP2**: (Tang et al., 2020a) - invited to participate in the "Dementia in Primary Care" collection.

Chapter Five presents qualitative research on the views of patients, their family carers and healthcare professionals on the current care pathway for post-stroke memory difficulties. This chapter includes **PP3:** (Tang et al., 2017a) and **PP4:** (Tang et al., 2018c)

Chapter Six presents both qualitative and quantitative assessments on the suitability of risk prediction models for dementia in stroke as a means to identify those at the greatest risk of post-stroke dementia earlier. This chapter includes **PP5:** (Tang et al., 2020b) and **PP6:** (Tang et al., 2019)

Chapter Seven provides evidence of expert consensus with regards to how best to manage post-stroke cognitive problems within the stroke service. This chapter includes **PP7:** (Tang et al., 2020c)

Chapter Eight is a summary discussion on the following: principal findings of the thesis, strengths and limitations of the studies, how the findings of this study relate to existing literature and clinical implications of the research findings and proposed future work.

Chapter 2: Current opportunities to ensure early detection of post-stroke dementia

2.1 The burden of stroke

Stroke itself is a leading global cause of both mortality and disability with high economic burden due to both treatment of the disease as well as post-stroke care (Rajsic et al., 2019). Although globally there have been substantial reductions in mortality rates from stroke, the overall burden of stroke remains high due to population ageing leading to an expanding proportion of older individuals (GBD 2015 Neurological Disorders Collaborator Group, 2017). In 2016, it was estimated that there were more than 80 million stroke survivors (GBD 2016 Stroke Collaborators, 2019). Greater numbers of stroke-survivors will also equate to higher numbers of individuals living with chronic stroke and its effects and also higher demands on post-stroke care.

According to a report in 2018 by the Stroke Association there are more than 100,000 strokes in the UK each year, which is around one stroke every 5 minutes (Stroke Association, 2018c). It is important to note that around 1 in 4 individuals will experience another stroke within 5 years (Stroke Association, 2018c). In community based samples, around 1 in 5 middle-aged women and 1 in 6 middle aged men will have a stroke in their lifetime (Seshadri and Wolf, 2007). Between 2015 and 2035, it has been projected that the incidence of stroke in the UK will increase by 60% per year and prevalence to increase by 120% (King et al., 2020). The aggregate annual costs of stroke care are estimated to be around £26 billion with unpaid care accounting for £15.8 billion (61% overall) and NHS care £3.4 billion (13%) (Patel et al., 2019). Although unpaid care reduces pressure and costs on formal services, we need to be mindful of the pressure this places on carers' and their own need for support to manage this responsibility (Patel et al., 2019). This has been projected to rise to £43 billion in 2025 and £75 billion in 2035 which represents an increase of 194% over 20 years (King et al., 2020).

To help with this, there is national guidance published by National Institute for Health and Care Excellence (NICE), which recommended that stroke-survivor's health and social care needs and the needs of their carers are reviewed at six months and then annually thereafter (National Insstitute for Health and Care

Excellence, 2013). This in theory is there to assist in the overall rehabilitation of the individual in terms of both physical, emotional and cognitive recovery.

2.2 Post-stroke cognitive deficits and dementia

Both stroke and dementia are defined as age-related diseases i.e. they are diseases with increasing incidence rates among the adult population (Chang et al., 2019). They are also related in that stroke is known to be a strong and independent risk factor for all cause dementia (Kuzma et al., 2018). Indeed, a previous systematic review and meta-analysis found that ten per cent of individuals developed dementia soon after their first stroke with more than a third suffering from dementia after recurrent stroke (Pendlebury and Rothwell, 2009). Further, the incidence of dementia a year after a major stroke is nearly 50 times higher than that in the general population (Pendlebury and Rothwell, 2019). It is also estimated that a stroke illness could accelerate the onset of dementia by 10 years (De Ronchi et al., 2007). Symptomatic stroke could therefore play a more prominent causal role rather than due to just the underlying vascular risk factors associated with both diseases.

2.3 Epidemiology of Post-Stroke Dementia

A number of different factors determine the overall prevalence of PSD including study setting (e.g. hospital vs. population-based studies), stroke type and severity and whether the individual has had recurrent stroke. A previous systematic review found that the prevalence of PSD ranged from 7% (population-based sample with pre-stoke dementia cases excluded) to 40% (hospital-based patients with recurrent stroke and pre-stroke dementia cases not excluded) (Pendlebury and Rothwell, 2009). A more recent meta-analysis looked at the prevalence of post-stroke neurocognitive disorders (NCD), and reported that major post-stroke NCD prevalence was 16.5% (95% CI: 12.1 – 20.8) (Barbay et al., 2018a). However, when mild and major NCD was defined according to other criteria (e.g. VASCOG criteria (Vascular Behavioural and Cognitive Disorders)), the prevalence of major NCD fell to 10.4% (95% CI 7.4 – 134) (Barbay et al., 2018b). However, it is clear from these studies that there needs to be a harmonised definition of post-stroke dementia (PSD) so that accurate cross-study comparisons can be made.

2.4 Defining Post-Stroke Dementia

Dementia is a syndrome that affects an individual's cognitive abilities and behaviour, and subsequently interferes with a person's ability to perform activities of daily living. Although dementia is traditionally viewed as causing a progressive and

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predictable loss of cognitive function, trajectories for deterioration may vary according to individual factors, underlying mechanisms and domains being assessed. The concept of vascular dementia (VaD) has traditionally been based on the multi-infarct model and ischaemic vascular disease (Hachinski et al., 1974). More recently, other criteria have been proposed for dementia in the context of vascular disease including 1) the National Institute of Neurological Disorders and Stroke – Association Internationale pour la Recherché et l'Enseignement en Neurosciences (NINDS-AIREN) (Roman et al., 1993); 2) State of California Alzheimer's Disease Diagnostic and Treatment Centers (ADDTC) (Chui et al., 1992); and, 3) The Diagnostic and Statistical Manual of Mental Disorders 4th Edition (DSM-IV) (American Psychiatric Association, 1994). Unfortunately, these criteria fail to allow for milder impairments outside of dementia. Further, memory is a pre-determining requirement to diagnose dementia in both NINDS-AIREN (Roman et al., 1993) and DSM-IV criteria (American Psychiatric Association, 1994). This is problematic as VaD patients tend to have superior function in verbal long term memory compared with AD patients (Looi and Sachdev, 1999). A broader term, namely vascular cognitive impairment (VCI) was introduced, which included all forms of cognitive impairment, from mild to severe, where the underlying cause is assumed to be due to cerebrovascular disease (O'Brien et al., 2003). Vascular dementia therefore sits on a continuum, which includes vascular cognitive impairment without dementia, vascular mild cognitive impairment and also dementia (O'Brien et al., 2003). VCI therefore encompasses those with cognitive impairments associated with a diverse cerebrovascular pathologies including lacunae, small-vessel disease with white matter lesions, multiple cortical and subcortical infracts and stroke (O'Brien et al., 2003). Specifically, at the time O'Brien and colleagues described PSD to include cases with multiple corticosubcortical infarcts, strategic infarcts, subcortical ischaemic vascular dementia and AD (O'Brien et al., 2003).

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Regarding PSD, there are numerous definitions. Henon and colleagues (Leys et al., 2005a, Henon et al., 2006) definition of PSD includes all types of dementias that occur after stroke irrespective of their cause. Mijajlovic and colleagues, based on the proceedings of the International Congress on Vascular Dementia (2015), defined PSD as any form of dementia which develops following a clinical cerebrovascular event (Mijajlovic et al., 2017). By defining PSD in this way there is no assumption about the underlying neuropathological cause as dementia post-stroke can comprise

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a mix of both vascular insults and neurodegeneration (Brainin et al., 2015, Mijajlovic et al., 2017). In the context of dementia, defining PSD can be challenging. One of the differentiating factors between cognitive impairment and dementia is usually based on limitations to activities of daily living (Sachdev et al., 2015). In the context of stroke, post-stroke physical sequelae may themselves lead to physical impairments without it being secondary to cognitive dysfunction. Further, as stroke and dementia tend to occur in older adults, one confounding factor may be that the stroke-survivor already had pre-existing diagnosed or undiagnosed cognitive impairment (Mijajlovic et al., 2017). It has also been suggested that the diagnosis of PSD should be delayed by at least 6 months after the event (Mijajlovic et al., 2017) as acute deficiencies in cognitive test scores may well improve when retesting in the short term (Wagle et al., 2010).

Other more recent definitions of PSD have a temporal relationship to stroke. For example, The Vascular Impairment of Cognition Classification Consensus study (VICCCS) defined PSD as a patient who exhibits immediate and/or delayed cognitive decline within 6 months of the stroke that does not reverse (Skrobot et al., 2017). Within this definition PSD is a subtype of the broader category of major VCI whereas VaD represents a severe form in the continuum of VCI. PSD is further subcategorised if a comorbid neuropathology is present, namely Alzheimer's Disease (AD), Dementia with Lewy Bodies (DLB) or other contributions (Skrobot et al., 2017).

A further set of criteria for vascular cognitive disorders was produced from the Congress of the International Society for Vascular Behavioural and Cognitive Disorders conferences in 2009 and 2013 (Sachdev et al., 2014). Vascular cognitive disorder is present if there is the presence of a cognitive disorder and vascular disease is determined to be the dominant if not exclusive underlying causative pathology for the cognitive disorder. Cognitive disorder is further divided into mild and major cognitive disorders, with major cognitive disorder being equivalent to dementia (Sachdev et al., 2014).

This thesis uses the definition proposed by Mijajlovic and colleagues, i.e. any form of dementia which develops following a clinical cerebrovascular event (Mijajlovic et al., 2017).

2.5 Screening and Case Finding for Dementia

Population screening looks to test asymptomatic individuals for a disease in order to increase earlier detection and therefore treatment of a disease (Maxim et al., 2014). However, at present, there is insufficient evidence to assess the benefits and harms in screening for cognitive impairment in asymptomatic individuals over the age of 65 years (Moyer, 2014). At present, the United Kingdom (UK) National Screening Committee (NSC) does not recommend universal screening for dementia (The UK National Screening Committee, 2019). The main reason being that there is no evidence of either accurate screening tests for dementia in those who have not already presented with symptoms nor are there effective treatments (The UK National Screening Committee, 2019). Screening for dementia raises complex issues for the public and clinicians and a systematic review of the literature has found that population screening for dementia may not be acceptable to either group (Martin et al., 2015b). In some cases, screening may identify individuals with symptoms but for various reasons have yet to present to a healthcare professional. Perceived lack of benefit, taboos surrounding dementia and the associated costs (including perceived financial motivations to implement screening) have been documented as barriers for patients and the public when it comes to population screening for dementia (Martin et al., 2015a). On the contrary, there is evidence that the greater the level of worry and concern about getting dementia can mean that they are more willing to be screened or tested for dementia (Tang et al., 2017b).

At present patients suspected of having a diagnosis of dementia, either because they or their caregiver are concerned about their memory or cognition, would present to their General Practitioner (GP) to undergo cognitive screening (Mate et al., 2017). The most recent NICE guideline recommended shorter cognitive tests such as the 10-point cognitive screener or the 6-item cognitive impairment test over tests such as the MMSE or the MoCA (Pink et al., 2018). Another approach is known as “case finding” i.e. offering investigation to identify the possible signs and symptoms of a dementia illness where the patient is at high risk of the disease and it may be of benefit to the patient (Ranson et al., 2018). It has been found that a case-finding approach could detect most people with dementia and presents the best opportunity for timely recognition of dementia in the community (Mate et al., 2017). This case finding approach consisted of either the clinical judgement of the GP or based on their answers to four questions in relation to the patient’s memory or

cognition concern and their disclosure or intent to disclose to their GP (Mate et al., 2017). In the UK, active case finding has been implemented previously in the community, seeking to opportunistically identify at-risk patients based on for example vascular risk factors, Parkinson's disease and learning disabilities (National Health Service (England), 2015). A similar hospital based approach (the National Dementia CQUIN) was also implemented to case find amongst those aged over 75 who were admitted as an emergency to either hospital or community services without a previous diagnosis of dementia (National Health Service (England), 2014). In the United States, the Medicare Annual Wellness Visit has also been used to detect any cognitive impairment if the individual shows signs or symptoms of cognitive impairment or if there are concerns raised by family members, friends, caregivers and others (Cordell et al., 2013). However, it can be argued that due to the subtle differences between case finding and screening, case finding is simply screening without an evidence base to protect the public against false positives or negatives (Cordell et al., 2013). In the context of stroke, stroke-survivors would certainly have met the criteria for the previous primary care enhanced service as older stroke-survivors would be classed as "at-risk" (National Health Service (England), 2015), but this service was dropped in 2016 as it was felt that GPs were more routinely diagnosing dementia (https://www.england.nhs.uk/2016/02/gp-contract-16-17/). Indeed, based on current gaps in evidence, there are recommendations against dementia case-finding in clinical practice (Ranson et al., 2018).

2.6 Screening for Post-Stroke Cognitive Decline

Cognitive impairment following a stroke is common (Jaillard et al., 2009) and is strongly associated with quality of life following a stroke (Cumming et al., 2014). A recent meta-analysis found that 40% of patients display some degree of cognitive impairment (no dementia) in the first year following a stroke (Sexton et al., 2019). There is currently no gold standard cognitive assessment in the context of stroke. A recent systematic review looked at various cognitive screening tools to differentiate vascular cognitive impairment and VaD from controls. In terms of screening tools, they found that the Montreal Cognitive Assessment (MoCA) test could reliably and accurately distinguish between controls and both VaD and Vascular Mild Cognitive Impairment (VMCI) (Ghafar et al., 2019). A number of cognitive screening tools are currently in use (see table 1). In a study, when screening tools were compared, there was no clear superior test for use in stroke settings although again the MoCA

displayed high sensitivity with a short assessment time (Lees et al., 2014). It should be noted however that many post-stroke cognitive deficits for example aphasia or visual problems are not so readily picked up by routine cognitive tests. Further, time of day also seems to affect cognitive performance when MoCA was used in older adults in the context of TIA and stroke (Mazzucco et al., 2017). A short cognitive screen, the Oxford Cognitive Screen (OCS), has been developed specifically for stroke patients which can be completed in 15-20 minutes and takes into account post-stroke domain specific impairments such as aphasia and neglect (Demeyere et al., 2015). When the OCS was compared against the Mini Mental State Examination (MMSE), the OCS found a much higher incidence of cognitive deficits post-stroke with the discrepancy particularly strong for those with milder strokes (Mancuso et al., 2018). Further, the OCS was found to detect high incidences of cognitive impairments specific to stroke which were not detected by the more traditional MMSE (Mancuso et al., 2018). The OCS also translates well across other e.g. Chinese and Russian populations (Hong et al., 2018, Shendyapina et al., 2019, Valera-Gran et al., 2019).

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Table 1. Comparison of Different Cognitive Tests

Cognitive Test Score	Cognitive Domains Tested	Time for Completion	Original Purpose
Mini-Mental State Examination (Folstein et al., 1975)	• 6 cognitive domains tested (visuospatial, language, concentration, working memory, memory recall, orientation) (Cameron et al., 2013)	10 minutes	To detect Alzheimer's dementia
Montreal Cognitive Assessment (Nasreddine et al., 2005)	• 8 cognitive domains (visuospatial skills, executive functions, language, attention, concentration, working memory, memory recall and orientation) (Cameron et al., 2013)	10 minutes	To detect mild cognitive impairment

Oxford Cognitive Screen (Demeyere et al., 2015)	• 10 tasks, five cognitive domains (attention and executive function, language, memory, number processing and praxis). • Brief evaluation of visual field defects	15 minutes	To describe cognitive deficits after stroke
Cognitive Assessment scale for Stroke Patients (CASP) (Barnay et al., 2014)	• Nine items evaluating 6 cognitive functions (language, praxis, short-term memory, temporal orientation, spatial/visuo-construction neglect and executive functions)	13 minutes	For cognitive disorders post-stroke adapted for administration to aphasic patients with verbal expression impairments.

2.7 Benefits of Earlier Identification of Cognitive Failure and Dementia

The World Alzheimer Report (2011) has previously highlighted the importance of an early dementia diagnosis (Pollock et al., 2012). To further qualify this, it has been proposed that the diagnosis of dementia should be "timely" (De Lepeleire et al., 2008), responding to concerns raised by the older person and their family rather than screening for early signs or symptoms of dementia (Prince et al., 2011). Timeliness is not dictated by *when* in terms of chronological time but rather the "right" or opportune time (Dhedhi et al., 2014). Despite the implementation of national dementia plans with commitment to early detection and diagnosis (Gardner S. O. and Splaine Consulting., 2017), a European survey reported that, from the perspective of family carers, timely diagnosis of dementia is found in only about half of cases (Woods et al., 2019).

A previous systematic review identified nine studies looking at the benefits and challenges of a timely diagnosis of confirmed AD, however, none of these studies specifically looked at diagnosing prodromal AD (Dubois et al., 2016). Some of the shared benefits include planning of future care, reduction in overall costs of dementia

and postponing institutionalisation (Dubois et al., 2016). For the patient timely diagnosis of AD could also reduce anxiety by addressing concerns about the individual's early symptoms and subsequent earlier access to treatment (Dubois et al., 2016). For the family and caregivers, it can provide answers to their concerns and enables access to support and resources that could reduce caregiver strain (Dubois et al., 2016). Certainly, barriers to timely diagnosis include stigma (Gauthier et al., 2013, Dubois et al., 2016) and whether it is appropriate to diagnose people in the initial symptomatic stages of the illness given the lack of effective treatments (Dubois et al., 2016). However, there seems to be more positivity around an earlier diagnosis of dementia. A recent study in Australia, reported that a significant majority (92%) of young and older adults preferred a diagnosis of dementia to be disclosed as soon as possible (Watson et al., 2018). Even though cultural differences may influence early detection of dementia (Lee et al., 2011), a separate cohort from Hong Kong also favoured wanting to know the diagnosis of dementia as soon as possible (Lam et al., 2019).

2.8 Risk Prediction Models Used to Assist in Earlier Diagnosis

2.8.1. Risk Prediction Models Used in Medicine

Understanding prognosis or risk in developing a disease is a common area in clinical research particularly as it may enable individuals to make lifestyle changes and plan ahead for their future personal circumstances. Indeed, whether or not an individual develops an illness or complications associated with the illness can depend on a number of different individual factors. This can be a mixture of demographic (e.g. age, education level and sex), social (e.g. smoking and alcohol history), health-related (e.g. history of certain medical conditions), genetic or even radiological factors. Given the heterogeneity and variability amongst individuals, it would be unlikely that a single predicting variable would be able to provide an accurate level of prognosis or risk hence the need for "multivariable research" (Moons et al., 2009). There is therefore a desire to include biomarkers or disease-specific variables to improve the specificity and sensitivity of these models.

Clinical risk prediction models, risk score or prognostic models typically use a variety of different patient specific variables in order to predict health outcomes over time (Moons et al., 2009, Pavlou et al., 2015). Common outcomes can be the development of a disease, death or complications. These models therefore enable the clinician to provide an estimate of an absolute risk or probability that this outcome

will occur in this individual (Moons et al., 2009). These estimates can then be used to guide and inform individuals on not only the possible prognosis or development of the disease but also to assist with treatment decisions.

There are numerous risk prediction models that have been developed for both research and clinical use. Examples include respiratory (e.g. outcome in chronic obstructive pulmonary disease (Bellou et al., 2019), childhood asthma (Smit et al., 2015)), emergency medicine (Brink et al., 2019), cardiovascular (e.g. heart failure (Di Tanna et al., 2020, Sahle et al., 2017), atrial fibrillation outcomes (Deng et al., 2017)), obstetrics (e.g. to predict for preeclampsia (De Kat et al., 2019)) and cancer (e.g. prognostic outcomes for pancreatic cancer (Bradley et al., 2019), survival in prostate cancer (Thurtle et al., 2019), breast cancer (Louro et al., 2019), liver cancer recurrence after transplantation (Al-Ameri et al., 2020)), transplantation (e.g. survival after heart transplantation (Aleksova et al., 2019). There have also been comparisons between different methods of modelling e.g. logistic regression versus machine learning (Christodoulou et al., 2019).

In terms of model performance, a model needs to be able to discriminate accurately between those who have the desired outcome and those without. The ability to stratify with sufficient probability can assist with clinical management decisions. Measures of discrimination include the concordance statistic and the area under the receiver operating characteristic curve (Steyerberg et al., 2010). A perfect model would therefore have an area of 1 (Steyerberg, 2009) with prognostic models typically between 0.6 and 0.85 (Royston et al., 2009). In general, a poorly discriminating model would probably have a c-statistic of 0.6 and a well discriminating model would have a c-statistic of 0.8. However, this should not be the only determining factor when choosing a risk prediction model (Steyerberg et al., 2010).

2.8.2. Commonly Used Clinical Risk Prediction Models

In terms of clinical usage, these have generally been in cardiovascular and cerebrovascular disease. The most well-known model that is routinely used in clinical practice, particularly in primary care, are the QRISK models to predict 10-year cardiovascular disease risk. The first QRISK model was developed in 2007 (Hippisley-Cox et al., 2007), with the updated QRISK2 published in 2008 and has been continually updated to reflect the changes in population characteristics (Hippisley-Cox et al., 2008). The models have been well validated in independent

cohorts (Collins and Altman, 2009, Arts et al., 2015, Pike et al., 2016, Collins and Altman, 2012) and QRISK2 is recommended in national guidance used across the NHS particularly with regards to lipid modification (Robson, 2008, National Institute for Health and Care Excellence, 2014, Health Improvement Scotland, 2017). In the field of cerebrovascular disease, models such as the ABCD2 score have been used to risk stratify individuals. ABCD2 uses variables such as age, blood pressure, clinical features of a transient ischaemic attack (TIA), duration of symptoms and a history of diabetes to determine who are at high risk of stroke following a TIA (Johnston et al., 2007). This model had previously been included in national guidance for stroke management, which dictated in particular how soon the patient should receive specialist assessment (National Institute for Health and Care Excellence, 2008). In the original development and validation paper, the c-statistics score varied from 0.62 – 0.83 (Johnston et al., 2007). In 2010, the ABCD2 was further improved by including the presence of ≥2 TIA symptoms within 7 days to the original score and termed ABCD3 (Merwick et al., 2010). Further improvement could be gained by including imaging variables such as carotid stenosis and abnormal acute diffusion-weighted imaging i.e. ABCD3-I (Merwick et al., 2010).

This guidance has recently been updated to reflect up to date evidence which has found that risk prediction scores (such as ABCD2 and ABCD3) when used by themselves do not discriminate high and low risk individuals well enough for it to be used (National Institute for Health and Care Excellence, 2019). Although the additional imaging variables do improve prediction, these are not readily found in primary care. However, there is evidence that the additional neuroimaging variables have been found to predict long term stroke risk after TIA (Kiyohara et al., 2014). Based on this evidence, it was felt that immediate specialist assessment would result in better health and economic outcomes for the entire TIA population without using this risk stratification tool (National Institute for Health and Care Excellence, 2019). This reversal in the use of a risk prediction tool in national guidance highlights the importance of thorough validation and testing prior to implementation particularly when you consider the original score's relatively modest range of discrimination scores.

2.8.3 Examples of Dementia Risk Prediction Scores

One of the most heavily researched risk models is the population based Cardiovascular Risk Factors, Aging and Dementia (CAIDE) score with 20 years of

follow-up (Kivipelto et al., 2006). The first model consists of both modifiable and non-modifiable variables (see table 2). The second model is model 1 with APOE ε4 status. The AUC for model 1 was 0.77 (95% CI 0.71 – 0.83) and model 2 was 0.78 (95% CI 0,72 – 0.84). The CAIDE score has been externally validated with similar levels of accuracy in midlife populations (36.1 years follow-up) (C statistic 0.75) (Exalto et al., 2014) but less accurate when shorter follow-up duration (10 years) was used (Licher et al., 2018b). A higher CAIDE score has also been associated with increased risk of cerebral infarcts (Hooshmand et al., 2018), related to MRI indicators of cerebrovascular changes and neurodegeneration (Stephen et al., 2017) including more severe white matter hyperintensities (Vuorinen et al., 2015). An App has also been developed using the CAIDE score to encourage users to actively reduce the risk factors which they are able to modify to potentially postpone the onset of cognitive impairment and dementia (Sindi et al., 2015). One of the most important uses of the CAIDE score to date has been its application in the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) trial (Ngandu et al., 2015). The FINGER trial aimed to use a multidomain intervention (diet, exercise, cognitive training, vascular risk monitoring) in those with a CAIDE score of at least 6 points and cognition at mean or slightly lower than that expected for age (Ngandu et al., 2015). This 2-year intervention trial found that this intervention could improve or maintain cognitive function in an at-risk elderly population (Ngandu et al., 2015). This methodology has now spread internationally (Rosenberg et al., 2020). From the FINGER trial, there seems to be some benefits in both global cognition and domain-specific cognition with plans for a 7 year extended follow-up to assess whether the intervention had any effects on dementia and Alzheimer's disease incidence (Ngandu et al., 2015). Within the context of stroke, the effect is unclear as only 5% of the intervention group reported a history of stroke and no stratified analyses was done (Ngandu et al., 2015).

Some models have looked at using modifiable variables either on its own or in the majority of variables used in the model with a view to enable an individual to potentially modify and lower one's risk for a dementia illness. This is because around a third of Alzheimer's diseases cases worldwide may be attributable to potentially modifiable factors (Norton et al., 2014). The Australian National University AD Risk index (ANU-ADRI) is an example of a self-report risk index that was developed using an evidence-based medicine approach (Anstey et al., 2013, Anstey et al., 2014). The

model contains 11 risk factors and four protective factors (see table 2) (Anstey et al., 2014). Three cohort studies were used in the validation of the model with a follow-up time ranging from 3.5 years to 6 years (Anstey et al., 2014). When assessing predictive accuracy of the models the C-statistics ranged from 0.637 – 0.740; when common variables were used (age, sex, education, diabetes, smoking and alcohol), the C-statistics were 0.666 – 0.734 (Anstey et al., 2014). When the model was externally validated for 10-year dementia risk the C-statistics for risk prediction was 0.75 but was similar to a model using age alone (C-statistic 0.77) (Licher et al., 2018b).

A similar approach was used for the Lifestyle for Brain Health (LIBRA) score (Deckers et al., 2015). This is a model developed from both systematic review of available literature and also Delphi consensus from experts (Deckers et al., 2015). The score consists of twelve modifiable risk factors and protective factors (see table 2) (Deckers et al., 2015). The score has been validated in midlife populations, which found that higher LIBRA scores were associated with higher dementia risk up to 30 years later (Deckers et al., 2020). However, when the model was tested in a large population dataset with 16 years follow-up, the AUC was only 0.60 (Schiepers et al., 2018). When they added education to this model, the AUC was 0.59; when education, age and sex were added the AUC was 0.75 (Schiepers et al., 2018). The benefit of a model containing modifiable risk factors means that it might enable the at-risk individual to modify their overall risk by making the necessary lifestyle changes. However, the overall accuracy of these variables seems to be lower than those where non-modifiable variables have been used. It also highlights the importance of age in these dementia risk models as a significant predictor, given that age alone models can perform just as well as these other models (Licher et al., 2018b).

There have also been disease-specific models in particular for diabetes. The type 2 diabetes-specific dementia risk score (DSDRS) was one of the first models created for diabetics to predict dementia (Exalto et al., 2013). This model was found to be able to predict dementia in diabetics at 10 years using a mixture of non-modifiable variables such as age and education alongside some diabetes specific variables (see table 2) (Exalto et al., 2013). The C-statistic for the development cohort was 0.736 and 0.746 for the validation cohort (Exalto et al., 2013) and has been recommended for patients with diabetes (Hou et al., 2019). A further model was

developed to predict dementia for Chinese type 2 diabetic patients where the following variables were used: age, sex, duration of type 2 diabetes, body mass index, variation in fasting plasma glucose and HbA1c, stroke, hypoglycaemia, postural hypotension, coronary artery disease and ant-diabetes medication (Li et al., 2018). The model was able to accurately predict dementia in diabetic populations with the following follow-up duration and AUC's: 3 years =0.82 (development), 0.84 (validation), 5 years = 0.79 (development) 0.80 (validation), 10 years = 0.76 (development), 0.75 (validation). A further model has been developed in those with diabetes and hypertension with good discriminatory accuracy (c-statistics 0.806 (95% CI 0.799 – 0.812) (Mehta et al., 2016). From these studies we can see that perhaps there are benefits when including variables that are disease-specific such as diabetic complications in the context of diabetics being at risk of dementia.

Table 2. Comparison of Common Dementia Risk Models

	Non-Modifiable Variables	**Modifiable Variables**
Cardiovascular Risk Factors, Aging and Dementia (Kivipelto et al., 2006)	Age Education Sex (APOE ε4 status)	Systolic blood pressure Body mass index Total cholesterol Physical activity
Australian National University AD Risk index (Anstey et al., 2013, Anstey et al., 2014)	Age Sex Education	Diabetes Traumatic brain injury Depressive symptoms Smoking Low social networks Cognitively stimulating activities Alcohol Physical activity Fish intake

Lifestyle for Brain Health (Deckers et al., 2015)		Renal disease Physical inactivity Smoking Obesity Hypertension Depression Diabetes Coronary heart disease Hypercholesterolaemia; Alcohol intake Diet Cognitive activity
Type 2 diabetes-specific dementia risk score (Exalto et al., 2013)	Age Education	Acute metabolic event, Microvascular disease Diabetic foot Cerebrovascular disease Cardiovascular disease Depression
Model from the Health Improvement Network (Walters et al., 2016)	Age Sex Social deprivation	Smoking BMI Heavy alcohol use Anti-hypertensive drugs Diabetes Stroke/TIA Atrial fibrillation Aspirin Depression

Brief Dementia Screening Indicator (Barnes et al., 2014)	Age Education	BMI History of type 2 diabetes History of stroke Needs help from others to manage money or medications Antidepressant medications or reports that "everything was an effort" for 3 or more days per week over the past week.

Some clinical risk prediction models have become routinely implemented for use in primary care for example cardiovascular risk prediction models to assist primary care clinicians when deciding on anti-cholesterol treatment (National Institute for Health and Care Excellence, 2014). Some dementia risk prediction models have been designed with primary care use in mind, for example by utilising data from primary care records. In a model using primary care routinely collected data (see table 2 for variables), it was found that in people aged 60-79 years this was model was able to accurately predict dementia at 5 years (C-statistic 0.84) but not for those aged over 80 years (Walters et al., 2016). A further model was developed and validated as a brief dementia screening indicator for primary care by Barnes and colleagues (Barnes et al., 2014). Four studies (the Cardiovascular Health Study, the Framingham Heart Study, the Health and retirement Study and the Sacramento Area Latino Study on Aging) were selected and predictive factors were chosen that were available in all or most of the cohorts and would be readily available or easily accessible in primary care (see final variables selected in table 2) (Barnes et al., 2014). The C-statistics ranged from 0.68 – 0.78 but did only include those aged between 65 – 79 (Barnes et al., 2014).

Overall, there is great variation in the overall accuracy of these models. Although there have been moves towards trying to use mainly modifiable variables so that an individual can modify their risk, models containing non-modifiable variables tend to be perform better, particularly when age is included.

2.9 The Challenges of Dementia Diagnosis in Primary Care

In the UK, GPs are the first point of contact for patients and their families who are concerned about their memory and/or cognitive abilities. GPs therefore have a key role in symptom recognition, investigation, initial cognitive screening and subsequent referral to specialist services to gain access to anti-dementia drugs (National Institute for Health and Care Excellence, 2018). However it is estimated worldwide that over 60% of dementia remains undiagnosed in the community and/or residential/nursing care, although the studies included in this systematic review were mainly from high-income countries (Lang et al., 2017). Factors associated with under detection may be to do with low socioeconomic levels for example in China (Chen et al., 2013), although this was not universally true as the same was not found in North America (Lang et al., 2017). In the UK, the undetected rate of dementia ranged from 42% in the community (O'Connor et al., 1988) and 32% (Lithgow et al., 2012) to 53% (Collerton et al., 2009) in the setting of residential/nursing care or mixed community and residential settings. In the meta-analysis it was found that there was increased undetected dementia if the diagnosis was made by GPs (Lang et al., 2017). Lack of support, time and financial constraints and diagnostic uncertainty have been cited as barriers to dementia diagnosis in primary care (Koch and Iliffe, 2010). In the UK, to improve detection rates and management of dementia in primary care, educational interventions have been trialled with some mixed success (Downs et al., 2006, Wilcock et al., 2013) with educational interventions being used in other parts of the world also (Schutze et al., 2018). The study by Downs and colleagues tested three education interventions: an electronic tutorial, decision support software and practice based workshops (Downs et al., 2006). Significant improvement in reported rates of dementia cases was obtained in the decision support software written inside the existing electronic medical record software and practice-based workshop groups (Downs et al., 2006). The trial by Wilcock and colleagues only used tailored practice-based workshops and did not improve dementia case identification (Wilcock et al., 2013). Finally, Schutze et al utilised a mixture of education programmes including small and large workshops and online modules but have yet to determine the long-term effects of their educational programme in terms of improving detection rates of dementia (Schutze et al., 2018). The intervention has found that participants could report improved knowledge, attitudes and practices and was found to be well received by its participants (Berenbaum et al., 2019). In the context of stroke, cognition and dementia, a similar programme and approach could be used to

heighten awareness to improve detection for a dementia illness in this at-risk group particularly for primary care healthcare professionals.

2.10 Chapter Summary

PSD is common but there is variation in how it is defined. There are challenges in how we screen and identify those who are at risk. These individuals may benefit from earlier intervention although the concept of a “timely” diagnosis of any dementia illness needs to take into account patient preferences. Upon discharge from stroke services, patients may face challenges when seeking a dementia diagnosis in the community. It is important to clarify to clinicians what the cognitive trajectory is following stroke so that they know when such individuals may present with symptoms suggestive of a dementia illness.

Chapter 3: Cognitive Trajectory Post-Stroke

This chapter presents findings from a systematic review of studies looking at how cognition changes over time following a stroke. Studies of stroke patients (≥50 years old) including two or more cognitive assessments over time were pooled together. By looking specifically at cognitive assessments, we can also look at the trends of how stroke affects different cognitive domains. This first publication explores the trends of cognitive scores over time and also looked at what variables could be associated with any subsequent cognitive impairment. This is particularly important for the subsequent studies looking at risk assessment for stroke-survivors for a future dementia illness.

3.1 What happens to cognition following a stroke?

There have been systematic reviews which examined all-cause dementia or study defined incident dementia as an outcome longitudinally (Kuzma et al., 2018, Savva and Stephan, 2010). One previous systematic review found that a history of stroke roughly doubles the risk of incident all-cause dementia in those aged >65 years (Savva and Stephan, 2010). This risk was independent of demographic and cardiovascular risk factors with more recent stroke leading to a greater association (Savva and Stephan, 2010). A more recent meta-analysis found that stroke was a strong risk factor for AD (risk ratio (RR) = 1.59, 95% Confidence Interval: 1.25 – 2.02). Finally, a meta-analysis was conducted for the relationship between stroke and all-cause dementia risk (Kuzma et al., 2018). Here, across eight studies, the pooled estimate found that incident stroke more than doubled the risk of all-cause dementia (RR = 2.18, 95% CI 1.90-2.50) (Kuzma et al., 2018). Similarly the pooled hazard ratio for prevalent stroke for all-cause dementia was 1.69 (95% CI: 1.49 – 1.92) (Kuzma et al., 2018). These studies focussed on dementia as an outcome. However, it is important to look at long-term trajectories of test scores that also include cognitive deficits either globally or within specific domains. It may well be that over time some cognitive domains stabilise or indeed recover, or some cognitive domains are more readily affected in the immediate post-stroke setting. Further, the factors associated with decline, stability or recovery will be important to determine particularly if they are modifiable variables to reduce overall risk.

3.2 PP1. Longitudinal Effect of Stroke on Cognition: A Systematic Review

Tang EYH, Amiesimaka O, Harrison S, Green E, Price C, Robinson L, Siervo M, Stephan B. (Journal of the American Heart Association); 2017: 7(2). pii: e006443

SYSTEMATIC REVIEW AND META-ANALYSIS

Longitudinal Effect of Stroke on Cognition: A Systematic Review

Eugene YH Tang, MSc; Obreniokibo Amiesimaka, BSc; Stephanie L Harrison, PhD; Emma Green, MSc; Christopher Price, MD; Louise Robinson, MD; Mario Siervo, PhD; Blossom CM Stephan, PhD

Background—Stroke is associated with an increased risk of dementia; however, the impact of stroke on cognition has been found to be variable, such that stroke survivors can show decline, remain stable, or revert to baseline cognitive functioning. Knowing the natural history of cognitive impairment after stroke is important for intervention. The aim of this systematic review is to investigate the longitudinal course of cognitive function in stroke survivors.

Methods and Results—Three electronic databases (Medline, Embase, PsycINFO) were searched using OvidSP from inception to July 15, 2016. Longitudinal studies with ≥2 time points of cognitive assessment after stroke were included. In total, 5952 articles were retrieved and 14 were included. There was a trend toward significant deterioration in cognitive test scores in stroke survivors (8 studies). Cognitive stability (3 studies) and improvement (3 studies) were also demonstrated, although follow-up time tended to be shorter in these studies. Variables associated with impairment included age, ethnicity, premorbid cognitive performance, depression, stroke location, and history of previous stroke. Associations with *APOE*E4* (apolipoprotein E with the E4 allele) allele status and sex were mixed.

Conclusions—Stroke is associated with an increased risk of cognitive decline, but cognitive decline is not a consequence. Factors associated with decline, such as sociodemographic status, health-related comorbidity, stroke history, and clinical features could be used in models to predict future risk of dementia after stroke. A risk model approach could identify patients at greatest risk for timely intervention to reduce the frequency or delay the onset of poststroke cognitive impairment and dementia. **(*J Am Heart Assoc*. 2018;7:e006443. DOI: 10.1161/JAHA.117.006443.)**

Key Words: cognition • cognitive impairment • dementia • risk factors/global assessment • stroke

Stroke is the second most common cause of acquired cognitive impairment, which predisposes patients toward institutionalization, disability, increased mortality, and poorer quality of life.[1–3] With an aging population and a decline in mortality after stroke,[4] the rates of poststroke cognitive impairment will increase. Despite being as common as other neurological deficits, such as motor and sensory, cognitive impairment is often overlooked in the follow-up of stroke survivors unless they have progressed to dementia.[5] This may well be because these patients are able to maintain some level of personal independence despite poor cognitive recovery.[6]

It has been found that stroke survivors may show no cognitive deficits or may decline, initially decline and then improve, remain stable, or progress to dementia over time.[7,8] Mixed findings may be related to differences in the cognitive tests used and test timing, history of previous stroke, stroke location, large- and small-vessel disease, population sample (clinical versus population based), ethnicity, and the presence of neurodegenerative pathology.[9] Nevertheless, it is also possible that the initial poststroke cognitive state may reflect prestroke cognitive decline[10] or delirium.[11] There is a drive toward detecting long-term cognitive outcomes after stroke to explore prevention; however, a preferred testing strategy is lacking, making cross-study comparison difficult.[12]

The aim of this systematic review was to assess the longitudinal pattern of cognitive function in stroke survivors and to determine those factors associated with change over

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Accompanying Tables S1 and S2 are available at http://jaha.ahajournals.org/content/7/2/e006443/DC1/embed/inline-supplementary-material-1.pdf

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Clinical Perspective

What Is New?

- Cognitive outcome following a stroke is dependent on sociodemographic, health, and stroke-related risk factors and the timing of cognitive assessment.

What Are the Clinical Implications?

- Poststroke patients need to have their cognitive function followed up over time to ensure that cognitive decline is noted early.
- Known risk factors associated with poststroke cognitive decline could be incorporated into risk scores to ensure timely detection of poststroke cognitive decline.

time. Recognizing the natural history of cognitive impairment after stroke is vital for informing early treatment and preventative strategies.

Methods

The data, analytic methods, and study materials will be made available to other researchers for purposes of reproducing the results or replicating the procedure. This material can be made available by the corresponding author on reasonable request.

Search Strategy and Selection Criteria

This systematic review was undertaken in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement.[13] The review was registered with PROSPERO (CRD42014015018). Three electronic databases—Medline, Embase, and PsycINFO—were searched using OvidSP from inception to July 15, 2016; searches were restricted to human studies and articles published in English. Predefined and Boolean search terms were used, including *stroke, (cognit* or neuropsych*),* and *(progress* or longitudinal or decline or prospective).* Longitudinal studies with ≥2 time points of cognitive assessment after stroke were included. No distinction was made regarding the sampling framework (clinic, hospital, or population based), the number of strokes, or the timing of cognitive assessments after stroke or cognitive battery used. Studies in which baseline and subsequent incident stroke cases found at follow-up were analyzed together were included. No distinction was made regarding the mechanism of stroke, and studies were not excluded if stroke was not confirmed using neuroimaging. All participants were adults who were aged ≥50 years and free from dementia. Randomized controlled trials and cognitive rehabilitation studies were excluded. Studies in which the only outcome was a diagnosis of dementia were excluded because this was the subject of a previous review.[14] Studies were excluded if change in cognitive function over time in the stroke group was not reported (ie, studies that only compared cognitive outcomes in stroke patients versus controls were excluded). Studies were also excluded if they reported percentages of decline rather than actual test scores or did not report statistical comparison of change in cognitive performance over time.

Four authors (O.A., E.Y.H.T., E.G., and S.L.H.) independently searched the article titles and abstracts. If the article could not be rejected with certainty based on title or abstract alone, then the full text of the article was obtained. Discrepancies between authors were resolved by consensus, and if this was not possible, then they were resolved by a third author (B.C.M.S.). Four authors (O.A., E.Y.H.T., E.G., and S.L.H.) carried out evaluation of full-text articles. Consensus or a third author resolved disagreements. The reference lists of the full-text articles and any relevant reviews were searched for potential eligible references.

Data Extraction

Data extracted included study design, sample size, demographic characteristics, inclusion or exclusion criteria, definition of stroke, cognitive test battery, and results. Three authors (E.Y.H.T., S.L.H., and E.G.) extracted data independently, and any discrepancies were resolved through consensus or discussion with a third author (B.C.M.S.). Because of the heterogeneity in the study design (eg, variation in follow-up time, cognitive test battery used), a meta-analysis was not possible.

Results

Figure shows the results of the electronic search and article-selection process. The search identified 9365 articles, of which 3413 were duplicates and thus removed. After reviewing titles and abstracts, 238 articles were retained for full-text review. The main reasons for exclusion were that the study population age was <50 years, cognitive measures were not reported, and a cross-sectional design was used. Fourteen articles met the inclusion criteria.

Study Characteristics

Characteristics of the included studies and detailed cognitive outcomes are shown in Tables S1 and S2, respectively. The number of participants at baseline ranged from 50[15] to 1187.[16] Follow-up ranged from 3 weeks[17] to 6 years.[15,18,19] The cohorts included stroke-specific populations[17,20–23] and

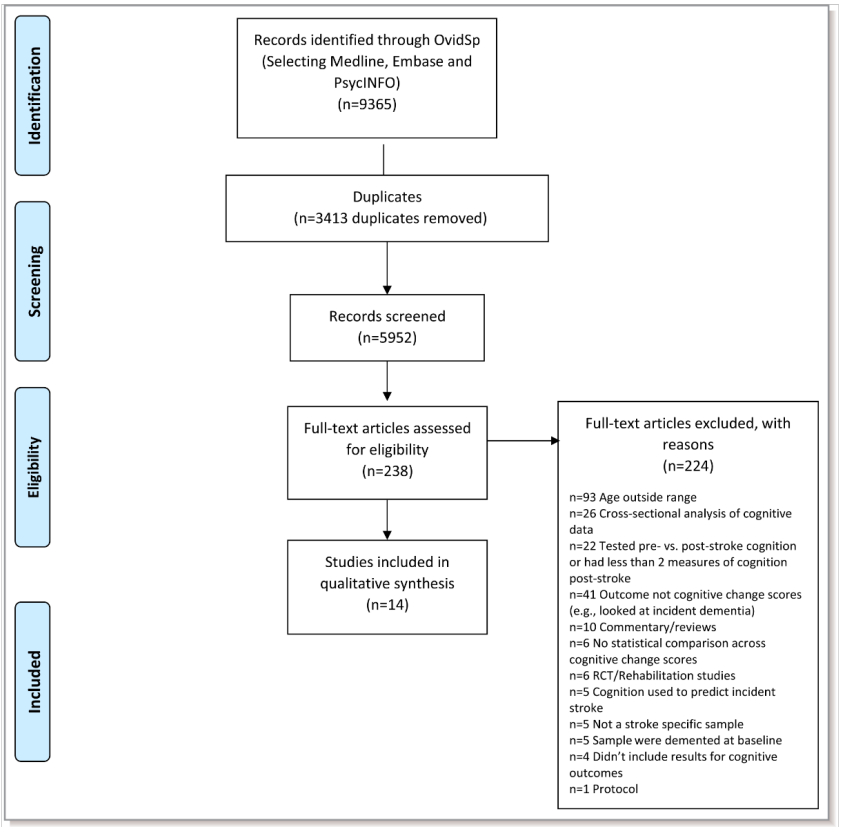

Figure. Flow diagram showing article selection. RCT indicates randomized controlled trial.

population-based studies.[15,16,18,19,24–28] The majority of studies were conducted in the United States (n=4),[16,18,25,26] followed by the United Kingdom (n=2),[20,27] Israel (n=2),[22,23] the Netherlands (n=2),[15,24] Germany (n=1),[19] India (n=1),[28] Norway (n=1),[21] and Japan (n=1).[17] Stroke case ascertainment included hospital-based diagnosis,[20–23,27] self-report,[15,25] general practitioner records,[19] self-report confirmed through medical records and/or expert review,[16,18,24,26,28] and not specified.[17] Only 2 studies used magnetic resonance imaging data.[22,23]

Cognitive Assessments

The Mini Mental State Examination (MMSE; total,[16,17,21,24,28] subtests scores,[26] and modified MMSE [3MSE][25]) was the most commonly used cognitive assessment. Other batteries for assessing global cognitive function included the Montreal Cognitive Assessment (MoCA),[22,23] the Cambridge Cognitive Assessment (CAMCOG),[27] the revised CAMCOG (CAMCOG-R),[20] and the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS).[21] Domain-specific

cognitive tests included the Auditory Verbal Learning Test (immediate and delayed recalled),[24] the Alphabet Coding Task,[15,24] East Boston Test,[16] the Symbol Digits Modalities Test,[16] subtests of the neuropsychological test battery of the Consortium to Establish a Registry for Alzheimer's Disease,[19] 2 subsets of Raven's Coloured Progressive Matrices,[15] and the word-list delayed recall of the Spanish and English Verbal Learning Test.[25] The computerized neuropsychological assessment NeuroTrax was used by 2 studies but in the same cohort.[22,23]

Study Sampling Framework

The majority of cohorts were population based (n=8),[15,16,18,19,24–26,28] although 5 studies were hospital based,[17,20–23] and the sampling framework was unclear in 1 study.[27] The studies demonstrating cognitive decline tended to be population-based cohorts with longer follow-up (3 years[28] to 6 years[15,18]). Studies demonstrating cognitive recovery were all hospital-based cohorts with shorter follow-up (3 weeks[17] to 13 months[21]). Cognitive outcomes were also reported in separate studies from the same population in 2 cohorts: a hospital-based cohort (Tel Aviv Brain Acute Stroke Cohort)[22,23] and a population-based cohort (Longitudinal Aging Study Amsterdam).[15,24]

Cognitive Function After Stroke

The impact of stroke on cognitive function over time was mixed as shown in the Table.

Global cognitive function

Most studies (n=12) included a measure of global cognitive function. Of these, 3 studies[16,18,28] reported significant decline (follow-up: 3–6 years), 3 studies[15,21,25] reported no change (follow-up: 13 months to 6 years), and 3 studies[17,20,21] reported significant improvement (follow-up: 3 weeks to 13 months) over time. In stratified analyses (4 studies), it was found (1) that although there was no significant decline in global function (3MSE score), over 3 years of follow-up in the whole sample with sex-stratified analysis, both men and women showed significant changes in 3MSE errors (worse in men than women, but no significant sex differences)[25]; (2) that stroke patients with slower physical performance, measured using the Timed Up and Go test, performed significantly worse on a computerized global cognitive test battery compared with stroke patients with faster physical performance (follow-up duration: 2 years)[22]; (3) that stroke patients with comorbid depression performed significantly worse on global cognitive scores compared with stroke patients without depression (follow-up duration: 2 years)[23]; and (4) that there was no significant difference in CAMCOG scores when stroke patients were stratified by homocysteine levels (follow-up duration: 27 months).[27]

Memory

Six studies included tests of memory.[15,19,21,24–26] Of these, 2 reported significant decline including impairments in immediate and delayed recall (follow-up: 6 years)[15] and visual memory (follow-up: 5 years).[29] Four studies reported no significant change in measures of verbal memory (follow-up: >3 years),[25] immediate memory (follow-up: 13 months),[21] or immediate and delayed recall (follow-up: 3.1–4.5 years).[19,24] One study found an improvement in delayed memory over 13 months of follow-up.[21] In stratified analyses, 1 study reported significant decline in memory for those with higher Geriatric Depression Scale (GDS) scores.[23] One study reported a significant decline in memory over 5-year follow-up and was also found to be strongest for men compared with women.[26]

Nonmemory

Five studies included nonmemory tests.[15,19,21,24,26] One study reported a significant decline in information processing speed over 6 years of follow-up.[15] Three studies reported no changes in nonmemory performance including measures of abstract reasoning,[26] visuospatial ability,[26] verbal fluency,[19] attention,[21] information processing speed,[24] and language performance[21,26] (follow-up: 13 months to 5 years). One study reported significant improvement in executive function over 3 months follow-up,[20] and another reported significant improvements in visuospatial/constructional performance over 13 months follow-up.[21] In stratified analysis, 1 study reported significant declines in executive function and visuospatial domains for those with higher admission and 6 month GDS scores; attention also declined in those who had higher GDS scores at 6 months.[23] A further study reported a significant decline in abstract/visuospatial scores in patients who were negative versus positive for *APOE*E4* (apolipoprotein E with the E4 allele).[26]

Risk Factors for Poststroke Cognitive Decline

Risk factors for cognitive impairment included ethnicity (greater risk in black patients compared with white patients),[16] depression,[23,28] increased age,[22,23,28] sex (mixed results[25,28]), *APOE*E4* status (mixed findings[21,24,26]), poorer cognitive performance after stroke,[22] stroke location (left and right hemisphere),[18] and a previous history of stroke.[21] Findings for sex were mixed: 1 study found no sex differences,[25] 1 found a greater risk of global impairment in women,[28] and another found a greater risk of decline in memory in men.[26] In 1 study, systolic blood pressure was not associated with global cognitive function >3 years after stroke in either men or women.[25]

Discussion

In this systematic review, the effect of stroke on longitudinal changes in cognitive function before a diagnosis of dementia

Table. Characteristics and Cognitive Findings From Included Studies (n=14)

Author	N	Sampling Framework	Follow-up	Cognitive Assessment	Key Findings	Risk Variables
Decline						
Cornijs, 2009[15]	50 T1, 90 T2, 84 T3	Population-based cohort	Maximum 6 y	MMSE, RCPM, ACT, AVLT (immediate and delayed recall)	Significant decline in memory (immediate and delayed recall) and information processing speed No significant change in global cognitive function	N/A
Rajan, 2014[16]	1187	Population-based cohort	Mean 4.2 y (SD 3.9)	East Boston Test (immediate and delayed story recall), Symbol Digits Modalities Test, MMSE (total and orientation scores)	Significant decline in global cognitive function	Increased risk of decline among black patients compared with white patients (all tests)
Ghosal, 2014[26]	283	Population-based cohort	Maximum 3 y	MMSE (Bengali version)	Significant decline in global cognitive function	Global impairment more common in women, higher age of onset of stroke, and people with higher depression scores
Levine, 2013[25]	151	Population-based cohort	Mean poststroke follow-up of 3.6 y for women and 3.4 y for men	Modified MMSE (3MSE), Word-List Delayed Recall of the Spanish and English Verbal Learning Test (SEVLT)	No significant change in global cognitive function or verbal memory No significant overall sex differences	No effect of systolic blood pressure on global cognition
Reitz, 2006[26]	97	Population-based cohort	Maximum 5 y	Orientation (MMSE items), Boston Naming Test, Controlled Word Association Test, category naming, Boston Diagnostic Aphasia Evaluation (Complex Ideational Material and Phrase Repetition), WAIS-R similarities subtest, nonverbal Identities and Oddities subtest of the Mattis Dementia Rating Scale, Rosen Drawing Test, Benton (matching), Benton Visual Retention Test and the Selective Reminding Test	Significant decline in memory No significant change in abstract/visuospatial or language	Significant decline in memory in men and abstract/visuospatial in *APOE*ε*4*-negative patients
Ben Assayag, 2015[22]	298	Hospital-based cohort	Maximum 2 y	MoCA and computerized global cognitive score (including memory, executive functions, visuospatial perception, verbal function, attention and motor skills)	Significant decline in global cognition in those taking longer to complete the TUG	Multivariable model: Age ≥75 y, TUG score >12 s at 6 mo after stroke, MoCA score 6 mo after stroke
Tene, 2016[23]	306	Hospital-based cohort	Maximum 2 y	As above	Significant decline in global cognition, memory, executive functioning and visuospatial in those with higher admission and six-month GDS scores; attention also declined in those who had higher GDS scores at 6 months	Multivariable model: MoCA score at hospital admission, age ≥75 y, GDS score ≥6 (admission and 6 mo after stroke)

Continued

Table. Continued

Author	N	Sampling Framework	Follow-up	Cognitive Assessment	Key Findings	Risk Variables
Toole, 2004[18]	5364	Population-based cohort	Maximum 6 y	3MS	Significant decline in global cognitive function	Left-hemisphere (highest decline) and right-hemisphere strokes
Stability						
Kohler, 2012[19]	3214	Population-based cohort	Maximum 4.5 y	CERAD verbal fluency and recall (immediate and delayed) tasks	No significant change in verbal fluency, immediate or delayed recall	Not reported
Rowan, 2007[27]	126	Unclear	Maximum 27 months	CAMCOG and the Cognitive Drug Research computerized battery	N/A	No significant decline in global cognitive function when stratified by homocysteine levels
Dik, 2000[24]	53	Population-based cohort	Mean 3.1 y (SD 0.2)	MMSE, AVLT (immediate and delayed), Coding Task (information processing speed)	No significant change in global cognition, memory, or information processing speed (adjusted models)	Lowered risk for global cognitive decline for *APOE*ε4* carriers (not significant)
Recovery						
Leeds, 2001[20]	83	Hospital-based cohort	Maximum 3 months	CAMCOG-R, Weigl color form sorting test, Raven's matrices	Significant improvement in global and executive function	Depression influenced executive function and CAMCOG-R scores
Wagle, 2010[21]	104	Hospital-based cohort	Mean 408.4 d (SD 41.2)	RBANS and MMSE	Significant improvement in visuospatial/constructional, delayed memory and global cognition (RBANS only) No significant change in global cognition (MMSE), immediate memory, language and attention	Multivariable model: Presence of *APOE*ε4*, prestroke cognitive reduction, previous stroke, and neurological impairment
Suzuki, 2013[17]	57	Hospital-based cohort	Maximum 3 wk	MMSE	Significant improvement in global cognitive function	Not reported

ACT indicates Alphabet Coding Task; AVLT, Auditory Verbal Learning Test; CAMCOG, Cambridge Cognitive Assessment; CAMCOG-R, Cambridge Cognitive Assessment (Revised); CERAD, Consortium to Establish a Register for Alzheimer's Disease; GDS, Geriatric Depression Score; MMSE, Mini Mental State Examination; MoCA, Montreal Cognitive Assessment; N/A, not assessed; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; RCPM, Raven's Colored Progressive Matrices; SEVLT, Spanish and English Verbal Learning Test; T, time point; 3MSE, Modified Mini Mental State Examination; TUG, Timed Up and Go; WAIS-R, Wechsler Adult Intelligence Scale-Revised.

was found to be mixed depending on the cognitive domain tested and methodology factors (eg, follow-up time). Furthermore, risk factors traditionally associated with cognitive decline, including *APOE*E4* status[24,26] and systolic blood pressure level,[25] did not have the same expected effect in stroke-specific samples. Accurate identification of stroke survivors at highest risk of cognitive decline is important and could be used to identify people for early intervention and participation in clinical trials.

Regarding global cognitive function, the majority of studies reported decline,[16,18,22,23,25,28] whereas 5 reported no change.[15,21,24,25,27] In contrast, 3 studies utilizing different cognitive batteries (MMSE[17], CAMCOG-R,[20] and RBANS[21]) reported recovery. Recovery as measured by MMSE and CAMCOG-R could be due to a combination of the small sample size of the study (57 patients[17] and 83 patients[20]) and short follow-up (3 weeks[17] and up to 3 months[20] after stroke). Furthermore, the study using the RBANS had a similarly small sample size (n=104) and short follow-up (13 months) and restricted the study population to those fulfilling requirements for rehabilitation, meaning that the study would have excluded the more severe strokes and thus potentially those at greater risk of cognitive decline.[21] When stroke survivors were followed up for a longer period of time (eg, ≥3 years), a significant decline in global cognition was reported.[16,18,28] Given that age is the biggest risk factor for incident dementia,[30] future studies could look at whether or not age of onset of stroke and disease duration determines the longitudinal cognitive trajectory after stroke. This would involve comparing stroke cohorts that had younger onset with an older stroke population and following their cognition over time. This approach could help describe global cognitive recovery in all stroke populations and assess who is at greatest risk of cognitive nonrecovery.

When assessing domain-specific function the results were mixed. Studies identified improvements in executive function,[20] visuospatial/constructional performance,[21] and memory (delayed)[21] over 3 to 13 months of follow-up. When participants were followed for longer periods (eg, ≥3 years), studies reported significant decline in memory (in some studies[15,26] but not all[18,23,28]) and no significant change in abstract/visuospatial performance.[26] Findings were mixed for information-processing speed, with 1 study reporting no significant change over 3 years of follow-up[24] but another reporting significant decline over 6 years of follow-up.[15] Two studies also found no significant change in language performance.[21,26] These mixed findings could be driven by varying sample size and heterogeneity in study design as well as by differences in the length of follow-up and medical treatments. These results highlight the importance of testing different cognitive domains in stroke survivors and the need to develop a consensus cognitive battery to allow cross-study comparison. Further work could assess the effect of stroke severity, subtypes, or locations on cognitive domains and factors that could assist in cognitive recovery.

Across studies, risk factors for cognitive decline included demographic factors (age, sex, ethnicity), neuropsychiatric symptoms (depression), disease-related comorbidity (previous stroke), poorer baseline cognitive tests, genetic factors (ie, *APOE*E4* status), function (balance and gait), and the nature of the stroke itself (stroke location). Factors such as arterial hypertension and the number of cerebral infarcts have been shown to be prognostic variables of cognitive deterioration.[31] However, not all factors were consistently observed to increase risk, including sex and *APOE*E4* status. With regard to sex, global impairment was found to be more common in women in 1 study,[28] which is comparable to existing literature.[32] In contrast, in another study, although there was no significant sex difference, global cognitive decline was found to be more severe in men.[25] However, this study was performed only in older Mexican Americans and may reflect only the relative risk found for this ethnicity. When specific domains were tested, when stratified by sex, men were found to show significant decline in memory.[26] However, the sample size for men was much smaller than that for women (n=27 versus n=70, respectively), which raises issues of statistical power. Regarding *APOE*E4* status, 1 study (n=19 who were APOE genotype 4/−) found a significant association between stroke and decline in abstract/visuospatial performance in those without the *APOE*E4* allele.[26] Another (n=27 *APOE*E4* positive)[24] found that stroke patients without the *APOE*E4* allele showed faster decline on global cognition, although this was not statistically significant and a synergistic effect was not observed.[24] In contrast, yet another study found that being an *APOE*E4* carrier was predictive of cognitive impairment at 13 months after stroke, but again, the sample size was small (n=25).[21] Given the inconsistency of these results with small sample sizes, further research is warranted to identify whether *APOE*E4* carriers with a history of stroke are at a higher risk of future poststroke cognitive impairment.

A number of risk scores have been developed to predict dementia in whole populations, with many using modifiable risk factors (eg, vascular risk factors[33,34]) with the hope that modifying these factors could alter cognitive trajectory. A risk model approach could be used in stroke populations, incorporating some of these variables identified in this review to predict poststroke dementia.[35] A number of risk scores have been developed recently to predict poststroke dementia (3 months after stroke, area under the curve: 0.74)[36] and cognitive impairment (6 months after stroke, area under the curve: 0.83).[37] Our review, however, shows that cognitive decline seems to become more apparent over a longer follow-up period, and thus new models could be developed to predict poststroke cognitive impairment and dementia over longer

time periods. Currently there are no specific biomarkers that can help discriminate between those at risk and those with better prognosis.[38] There is evidence, however, of a strong relationship between inflammation markers and cognitive performance,[39] and this will need further evaluation before being used in potential risk models. Although neuroimaging variables were used in the cognitive impairment model,[37] evidence shows that data from magnetic resonance imaging do not significantly improve prediction in all-cause dementia models.[40] Similarly, there may be less focus on incorporating vascular risk factors into these models because results from a recent clinical trial found that intensively managing vascular risk factors in stroke survivors did not alter cognition after 2 years.[41]

Strengths and Limitations

This study has a number of strengths. We performed a systematic search of all studies focusing on older aged samples. Furthermore, we did not restrict our search by cognitive domain. This is important in stroke samples, for which overall cognitive improvement may be explained by significant improvements in some nonmemory domains but individuals may still show persisting memory deficits. We also ensured that the included studies had statistical comparisons of change in cognitive test scores over time. Nevertheless, there are limitations. Only studies in English were included, and the majority of studies were in white populations. Consequently, the results may not extrapolate to nonwhite samples. Studies were also excluded if the sample baseline age was ≤50 years because stroke before age 50 is uncommon, and these patients may have a different risk profile than the older population.

Conclusions

Cognitive outcomes after stroke can be variable, and standardized assessment tools together with recommended time intervals for testing are needed. Determinants of poststroke cognitive decline are important to clarify, particularly if these patients are different from the nonstroke population; interventions may need to be tailored specifically to stroke survivors. A number of risk factors for cognitive decline, particularly in global functioning, in stroke survivors have been found, such as age, sex, stroke location, and medical comorbidities (depression), and could be incorporated into a risk tool to identify stroke survivors at highest risk of cognitive decline over short and long durations of follow-up.

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SUPPLEMENTAL MATERIAL

Table S1. Study Characteristics

Author, Year	Data Resource	Demographic Data	Frequency and Timing of Cognitive Assessment	Stroke Cases and Definition Reported
Comijs 2009[1]	LASA, population based study, the Netherlands (50 T1, 90 T2, 84 T3)	Mean age (total sample)=72.1 (Range: 55-85) Mean education (total sample)=9.0 years Male 51.5% (total sample)	Up to six years Time 1 = 1992-93, Time 2 = 1995-96, Time 3 = 1998-99	Self-reported
Rajan 2014[2]	Chicago Health and Aging Project Baseline n=1187	Mean age=73.7 years (SD=6.3) Mean (SD) Mean education=12.0 years (SD=3.4) Male 41%	Mean follow-up time after incident stroke was 4.2 years (SD=3.9).	Self-report ischaemic and haemorrhagic
Ghosal 2014[3]	Urban community in Kolkata 3 annual visits, baseline year (n = 283), first follow-up (n = 220), second follow-up (n = 181), third follow-up (n = 159)	Mean age (SD): 64.27 +/- 13.08 years Male 51.9% Female 48.9% Mean education (SD): 5.42 +/- 4.84 years	Bengali versions of the Mini Mental State Examination (BMSE); Baseline and 3 annual follow-up visits	Cases initially screened by field workers using a validated WHO-based questionnaire. Screened patients were further examined by field physicians and the findings reviewed by senior neurologists. WHO definition
Levine 2013[4]	Sacramento Area Latino Study on Aging (SALSA cohort) (1576, 151 with	Male (n=655, mean age=70.2, SD=6.7);	Yearly for ten years. Incident first-ever stroke mean years of follow-up: women 3.6 years, 3.4 for men	Participant self-report of a physician

	incident first-ever stroke during ten years of follow-up)	Female (n=921, mean age=70. Incident first-ever stroke: 72 +/- 8 years 655 Males, 921 Females. Incident first-ever stroke: 66 men, 85 women Male (n=655, mean education =8.0 years, SD=5.6); Female (n=921, mean education =6.9 years, SD=5.1); Education: First-ever stroke: male 7.6 (SD 5.6) years, female 7.0 (SD 5.9 years)		diagnosis during following up or stroke as cause of death on death report
Reitz 2006[5]	Longitudinal study of Medicare recipients in northern Manhattan (1271 (Stroke cases = 97))	Mean age = 76.2 years, SD=6.0 69.6% female Mean education = 8.6 yrs, SD=4.6	Baseline data (1992-1994), follow up data during sequential intervals of approximately 18 months (1994-1996, 1996-1997, 1997-1999) – 5 year interval.	Participant/ informant interview; confirmed by medical records (85% included brain imaging), remainder by direct exam WHO criteria
Suzuki 2013[6]	First round: 57, Second round 43	First round mean age 73.5 years (SD 9.3) Second round mean 72.4 (SD 10.8) First round Female 56.1% Second round Female 55.8%	Initial assessment from onset of stroke (baseline assessment) and then at 1 week (second set of assessments) and 2 weeks (third set of assessments) after the baseline assessment. Second round of data collection: baseline assessment and at 1, 2, and 3 weeks after the baseline assessment in each individual.	NOT REPORTED
Ben Assayag 2015[7]	Tel Aviv Brain Acute Stroke Cohort (TOBASCO) Study (n – 298)	Mean age 66.7+/-9.6 years 62.4% male (n = 186) Mean education 13.2 (SD 3.7) years	Baseline MoCA and NeuroTrax computerised cognitive testing and then repeated at 6, 12 and 24 months following the event. The average of the 6 index scores (memory, executive functions, visuospatial perception, verbal function, attention and motor skills) was computed as the global cognitive score.	Mild to moderate first-ever acute ischaemic stroke
Tene 2016[8]	Tel Aviv Brain Acute Stroke Cohort (TOBASCO) Study	Mean age (SD): 67.1 (10.0) years) n (%) males 182 (59.5)	Baseline MoCA and NeuroTrax computerised cognitive testing and then repeated at 6, 12 and 24 months following the event. The average of the 6 index scores (memory, executive functions, visuospatial perception, verbal	Mild to moderate first-ever acute

	Baseline = 306, 6, 12 and 24 month follow-up	Mean education (SD): 13.2 (3.7) years	function, attention and motor skills) was computed as the global cognitive score.	ischaemic stroke
Toole 2004[9]	Population based cohort (Cardiovascular Health Study) (n = 5364)	≥65	Follow-up visits between 1992- 1998	Self-report and confirmed by medical record
Kohler 2012[10]	Ageing, Cognition and Dementia in Primary Care patients (AgeCoDe), Germany (3214 at baseline, 321 cases)	Mean age (total sample)=79.7 (SD=3.6, range: 75-98) Education (as measured by the Comparative Analysis of Social Mobility in Industrial Nations classification): Low (1988) 61.9% Middle (883) 27.5% High (343) 10.7% Male 34.5% (total sample)	Three follow-ups, every 18 months after baseline (between 2003 – 2009)	Primary care based records - stroke or TIA
Rowan 2007[11]	N = 126	Median age=79.4 years Males – n=94 (55.3%)	3, 15 and 27 months post stroke	Clinical and CT scan evidence-based diagnosis of stroke Oxford community Stroke Project classification
Dik 2000[12]	LASA, the Netherlands 1,224 in total sample, 53 stroke patients	Age Range 65-85 years Stroke (n=53, Mean=74.6 years, SD=6.7). Stroke (male=37, 69.8%). Stroke (Mean education =8.5 yrs, SD=3.4).	Mean follow-up=3.1 (SD=0.2) years	GP diagnosis of stroke. When GP diagnosis not available participant self-report (n=211)

Leeds 2001[13]	Admissions to stroke rehabilitation unit (n = 83)	60+ years (Mean age=75.4 years, SD=8.1) 44 male, 39 female	1 month (mean=4.14 weeks, range 1-5 weeks) and 3 months post stroke	93 stroke confirmed by CT scan; rest based on clinical history and physical examination
Wagle 2010[14]	Admissions to stroke rehabilitation unit of Ulleval University Hospital (Oslo, Norway) (n = 104)	Cognitive impairment group (n=52, age mean=81.0 SD=9.5). No cognitive impairment group (n=52, age mean=78.0 SD=20.3) Cognitive impairment group (n=52, females=23, 44%). No cognitive impairment group (n=52, females=25, 47%) Cognitive impairment group (n=52, Mean education =11.0 years SD=5.0). No cognitive impairment group (n=52, Mean education =11.0 years SD=3.8)	12-15 months post stroke (Mean=408.4 days, SD= 41.2)	Ischemic or hemorrhagic

Abbreviations

ACT, Alphabet Coding Task; AD, Alzheimer's Disease; ADL, Activities of Daily Living; AVLT, Auditory Verbal Learning Test; BMSE, Bengali versions of the Mini Mental State Examination; CAMCOG, Cambridge Cognitive Assessment; Cambridge Cognitive Assessment ; CAMCOG-R, Cambridge Cognitive Assessment; Cambridge Cognitive Assessment (Revised); CERAD, Consortium to Establish a Register for Alzheimer's Disease; COGFAST, Cognitive Function After Stroke; CT, Computed Tomography; DSM, Diagnostic and Statistical Manual of Mental Disorders; GP, General Practitioner; LACI, Lacunar infarct; LASA, Longitudinal Aging Study Amsterdam; M, Mean; MMSE, Mini Mental State Examination; MoCA, Montreal Cognitive Assessment; MRC, Medical Research Council; NIHSS, National Institutes of Health Stroke Scale; PACI, Posterior anterior circulation infarct; POCI, posterior circulation infarct; RCPM, Raven's Colored Progressive Matrices; SD, Standard Deviation; TIA, transient ischaemic attack; WAIS-R, Wechsler Adult Intelligence Scale-Revised; WHO, World Health Organisation

Table S2 Baseline and Follow-up Cognitive Measures

Author, Year	Baseline Measures	Follow-up Measures	Grouped Results and Outcome
Comijs 2009[1]	Mean (±SD) General Cognitive Functioning (MMSE): T1 27.5±2.0 Fluid Intelligence T1 18.0±3.9 Information processing speed T1 24.3±6.9 Immediate AVLT T1 7.7±2.5 Delayed AVLT T1 5.1±2.6	Mean (±SD) General Cognitive Functioning (MMSE): T2 27.2±2.4 T3 27.2±2.4 Fluid Intelligence T2 17.6±4.0 T3 17.2±4.0 Information processing speed T2 23.3±7.1 T3 23.2±6.9 Immediate AVLT T2 8.0±2.7 T3 7.7±2.7 Delayed AVLT T2 5.7±3.0 T3 5.3±2.9	Interactions between time and stroke (mean differences in cognitive function) between those with and those without stroke Information processing speed (ACT) T1 -1.08, T2 -2.78, T3 -3.40 ($p < 0.05$) Immediate Recall (AVLT) T1 0.01, T2 -0.35, T3 -0.72 ($p<0.04$) Delayed Recall (AVLT) T1 0.10, T2 -0.41, T3 -0.92 ($p<0.005$) MMSE β=-0.26 (-0.69/0.16); RCPM β=-0.73 (-1.32/-0.14); ACT β=-1.97 (-2.78/-1.16); AVLT (immediate) b=-0.44 (-0.83/-0.06); AVLT (delayed) β=-0.56 (-0.95/-0.17) Compared to no-stroke, stroke had a higher rate of decline for information processing speed (p=0.05) and memory (immediate p=0.04, delayed p=0.005)
Rajan 2014[2]	MMSE Mean (SD): 26.3 (4.2) Delayed recall Mean (SD): 7.7 (3.0) Immediate recall Mean (SD): 8.3 (2.6) Symbols digit Mean (SD): 28.4 (13.7) Composite measure of 4 tests Mean (SD): 0.142 (0.753)	NOT REPORTED	Cognitive function decline increased by 0.058 units/year after incident stroke. Cognitive decline increased significantly after stroke relative to before stroke. Cognitive decline increased 1.9 fold after incident stroke with cognitive function predicting mortality even after adjusting for stroke, demographic and health related factors.
Kohler 2012[10]	No reported stroke only outcomes	NOT REPORTED	Verbal fluency (estimate, p-value): intercept -0.919, 0.002 slope -0.219, 0.56;

	Verbal fluency: M=19.5, SD=5.4. (Not stroke or TIA specific) Immediate recall: M=18.6, SD=4.0. (Not stroke or TIA specific) Delayed recall: M=5.4, SD=2.2. (Not stroke/TIA specific)		Immediate recall (estimate, p-value): intercept -0.641, 0.003; slope -0.532, 0.09 Delayed recall (estimate, p-value): intercept -0.311, 0.01; slope -0.062, 0.68
Ghosal 2014[3]	BMSE (n = 254) - mean (SD) 26.48 +/- 3.4	BMSE mean (SD) Year 1 (n = 197) 26.81 +/- 3.11 Year 2 (n = 161) 26.45 +/- 3.75 Year 3 (n = 141) 25.89 +/- 4.66	BMSE Coefficient time (standard error) over 3 years = -0.2061 (0.0937) (p = 0.028) Cognitive dysfunction was associated with negative outcome regarding mood state affecting both basic and instrumental activities of daily living. Education was inversely related to cognitive status. Neuropsychiatric (depression and cognition), socioeconomic (lower educational level), demographic (female sex), and cultural factors can adversely affect outcome in stroke survivors.
Levine 2013[4]	3MSE: men mean =83.3 (SD 12.1), women M=85.1 (SD 11.8) Word list delayed recall: men mean=7.0 (SD 2.9) women M=8.7 (SD 3.0)	3MSE errors increased by 22%/year in men (95% CI, 6.8% - 36.7%) and 13.2%/year in women (95% CI, 3.5% - 22.9%) Word list improved by 0.05 words/year (95% CI -0.24 - 0.33) in men and by 0.09 words/year (95% CI -0.16 - 0.34)	Parameter (SE), p value. 3MSE Men Model A post-stroke intercept: 0.60 (0.39), non-significant post stroke by time interaction term: 0.17 (0.06), p<=0.01 post stroke change per visit: 0.20 (0.06), p<=0.01 Model B post-stroke intercept: 0.29 (0.38), non-significant post stroke by time interaction term: 0.16 (0.06), p<=0.01 post stroke change per visit: 0.17 (0.06), p<=0.01 Women Model A post-stroke intercept: 0.71 (0.39), p<=0.05 post stroke by time interaction term: 0.09 (0.04), p<=0.05 post stroke change per visit: 0.12 (0.04), p<=0.01 Model B

			post-stroke intercept: 0.49 (0.28), non-significant post stroke by time interaction term: 0.12 (0.04), p<=0.01 post stroke change per visit: 0.13 (0.04), p<=0.01 Model A: included baseline age and years of education, time varying depressive symptoms (CES-D scores), time varying incident stroke, time and the incident stroke by time interaction term. Model B added time-varying systolic BP to model A. MMSE: 3MSE errors increased by 2.4% per year in men and increased by 3.3& per year in women. Post stroke changes in 3MSE errors were statistically significant in both men and women. Over the post stroke period 3MSE errors increased by 22% per year in men and by 13.2% per year in women. Changes in word list scores post-stroke were not statistically significant in either sex. However, the magnitude of post-stroke change in word list scores was 1.7 times larger in women than in men.
Dik 2000[12]	Mean MMSE 26.5 Mean Immediate recall 6.8 Mean delayed recall 4.1 Mean information processing speed 20.2	No scores published but percentage that declined reported: Decline in MMSE % 28.3% Decline in Immediate recall 11.8% Decline in delayed recall % 19.6 Decline in information processing speed % 18.8	Odds Ratio (95% CI) for Stroke patients (adjusted for age, sex, education, baseline cognition score) MMSE 1.9 (1.0-3.7) Immediate Recall 0.7 (0.4 – 1.6) Delayed Recall 1.4 (0.7 – 2.9) Information processing speed 1.2 (0.7 – 2.1) APOE e4 carriers demonstrated a non-significantly lowered risk for MMSE decline. APOE e4 associated with declines in info processing speed and small declines for immediate and delayed recall. Of the 53 stroke patients - (n=17) had the e4 allele for APOE, (n=36) did not. Stroke patients without ApoE e4 had the lowest changes in MMSE (-1.6 points). Stroke patients with e4 showed greater declines in info processing speed (-2.0 points).
Reitz 2006[5]	NOT REPORTED	NOT REPORTED	Memory declined significantly over time (β= -1.6, p=0.005), abstract/visuospatial and language performance remained stable. A history of stroke was associated with more rapid decline in memory performance over time (β=-3.6, p=0.04). There was no relation between stroke and decline in abstract/visuospatial or language performance. Memory and abstract/visuospatial function declined at a faster rate in men or persons who lacked the APOEe4 allele with stroke compared to women or APOEe4 carriers. This remain unchanged after adjusting for age, education, ethnic group, BMI< hypertension, heart disease, diabetes and smoking.

			The association between stroke and decline in memory performance was strongest for men and for persons without an APOE4 allele. A significant association between stroke and decline in abstract/visuospatial performance was also observed for persons without the APOE-e4 allele.
Suzuki 2013[6]	MMSE at baseline First round: median 23 (IQR: 17 - 25), Second round: median 23 (IQR 20 - 25)	MMSE (second round): third assessment (2 weeks) - Median 24 (IQR 22 - 27), fourth set of assessments median 25 (IQR 23-28)	Third set of Assessments Predicted MMSE Score (logarithmic model) median 25 (IQR 22-27), model fit 0.68 (P<0.0001 for difference between actual and predicted values). Predicted MMSE score (linear regression model): median 25 (IQR 22-28), Model fit 0.60 (P<00001 for difference between actual and predicted values (linear regression analysis)
Ben Assayag 2015[7]	Mean (SD) (Baseline) All participants: MoCA 23.9 (3.3) Cognitively intact at 2 years: 24.3 (3.1) Cognitive Decline 2 years after stroke: 21.8 (3.6) Mean (SD) (Baseline) All participants: Computerised global cognitive score 92.5 (14.1) Cognitively intact at 2 years: 93.6 (13.7) Cognitive Decline 2 years after stroke: 86 (15.2)	Mean (SD) (6 months) All participants: MoCA 25.3 (3.3) Cognitively intact at 2 years: 25.7 (3) Cognitive Decline 2 years after stroke: 22.9 (3.9) Mean (SD) (6 months) All participants: Computerised global cognitive score 94.8 (12.4) Cognitively intact at 2 years: 96.1 (11.8) Cognitive Decline 2 years after stroke: 87 (13.5)	Cognitive scores 6 months after stroke/TIA (23.9±3.3 versus 25.3±3.3, P<0.001 for the Montreal cognitive assessment scores; 92.5±14.1 versus 94.8±12.4, P<0.001 for the computerized global cognitive score Univariate predictors of cognitive decline 24 months from stroke include: age greater than or equal to 75, education <12 years, white matter lesion score, Modified Rankin score 6 months after stroke, MoCA score at hospital admission, MoCA score 6 months after stroke, Berg Balance Scale 6 months after stroke (<50), the Timed Up and Go test score 6 months after stroke (>12 seconds), number of correct answers during dual-task 6 months after stroke (<15). Multivariate predictors include age greater than or equal to 75 years, TUG score (> 12secs) 6 months after stroke, MoCA score 6 months after stroke Balance and gait are significant risk markers for cognitive status and impaired cognitive recovery after mild stroke or TIA
Tene 2016[8]	Mean (SD) (Baseline) All participants: MoCA 23.8 (3.3) GDS < 6: 23.8 (3.4) GDS > or equals 6: 23.5 (3.2) Mean (SD) (Baseline) All participants: Computerised global cognitive score 91.8 (14.1) GDS <6: 91.9 (14.6)	Mean (SD) (6 months) All participants: MoCA 25.0 (3.7) GDS < 6: 25.1 (3.5) GDS > or equals 6: 24.2 (4.6) Mean (SD) (6 months) All participants: Computerised global cognitive score 94.1 (12.5) GDS <6: 94.8 (12.1) GDS > or equals 6: 89.4 (14.1)	Univariate predictors of cognitive decline 24 months from stroke include: age greater or equal to 75 years, education <12 years, ischaemic heart disease, hypertension, white matter lesion score, MoCA score at hospital admission, MoCA score 6 months after stroke Computerised global cognitive score at admission and 6 months post-stroke, GDS score at admission and 6 months posts-stoke. Multivariate predictors include MoCA at admission, age greater or equal to 75 and admission GDS score greater than or equal to 6 Depressive symptoms in poststroke/TIA patients are associated with MCI or dementia and functional deterioration at 2-year follow-up. This association occurs immediately after stroke/TIA and becomes more significant 6 months after the initial stroke.

	GDS > or equals 6: 91.3 (9.3)		
Leeds 2001[13]	CAMCOG-R Baseline TOTAL: 79.5 (median), mean 77.8 (SD 13.8) EF: 14.0 (median), mean 13.1 (SD 4.7) EX: median 5.0, mean 5.1 (SD 2.6)	Follow-up – significant improvement in all three mean scores: TOTAL: 83.14 (SD 12.2) EF 14.6 (SD 4.9) EX 5.8 (SD 2.5)	Depression influenced the performance on executive function tests as well as the overall CAMCOG-R score.
Wagle 2010[14]	RBANS total scale score at baseline (median (IQR)): n=104, total score baseline 73 (20). (Cognitive impairment according to RBANS Total Index Score was defined as a score <= 77.5 points, equal to 1.5 SD below mean which is recommended cut-off score for MCI. MMSE score at baseline (median (IQR)): n=104. MMSE=25 (7) RBANs index score (individual tests) (median (IQR)): Immediate memory 89 (25) Visuospatial/constructional 82 (34) Language 76 (22)	RBANS total scale score at 13 months follow up (median (IQR)): n=104, total score follow up 78 (29) (p=0.001) MMSE score at 13 months follow up (median (IQR)): n=104. MMSE=25 (9) RBANS index score (individual tests) at 13 months (median (IQR)): Immediate memory 89 (39) Visuospatial/constructional 94 (45) Language 82 (25) Attention 65 (18) Delayed memory 83 (29) Significant differences found for visuospatial (p<0.001), delayed memory (p=0.034) APOEe4-negative RBANS index scores at 13 months (median (IQR)) Immediate memory 91.0 (36.0) Visuospatial/constructional 97.0 (46.0) Language 84.0 (25.0) Attention 70.0 (21.0)	Of the n=104, 61 (59%) were classified as cognitively impaired at baseline, compared to 52 (50%) at follow up. In total, 45 were classed as cog. Impaired at both occasions (persistent cases), 7 of the non-impaired at baseline switched to impaired at follow up, 16 were classed as cognitively impaired at baseline but switched to non-impaired at follow up (recovery cases) A significant dose-dependent effect of the APOE-genotype in relation to overall post-stroke cognitive functioning was found at baseline and follow-up, but not pre-stroke. The e4 carriers showed a significant decline in tests related to verbal learning and memory compared to the non-carriers. Four factors at baseline were independently associated with cognitive impairment at 13 months after acute stroke: Previous stroke, higher IQCODE score (indicating poorer pre-stroke cognitive functioning), higher NIHSS score (indicating more severe strokes) and the presence of one or two e4-alleles.

	Attention 70 (18) Delayed memory 82 (22) APOEe4-negative RBANS index scores (median (IQR)) Immediate memory 94.0 (23.0) Visuospatial/constructional 82.0 (33.0) Language 82.0 (23.0) Attention 70.0 (18.0) Delayed memory 85.0 (23.0) Total scale 77.0 (21.0) APOEe4 positive RBANs index score (median (IQR)) Immediate memory 83.0 (25.0) Visuospatial/constructional 78.0 (27.5) Language 71.0 (16.5) Attention 65.0 (11.5) Delayed memory 76.0 (14.5) Total scale 65.0 (11.5) APOEe4-negative MMSE (median (IQR)) Total 25.0 (7.0) Orientation for time 4.0 (2.0) Orientation for place 5.0 (1.0) APOEe4-positive MMSE (median (IQR)) Total 26.0 (8.0) Orientation for time 4.0	Delayed memory 91.0 (29.0) Total scale 83.0 (32.0) APOEe4 positive RBANs index score (median (IQR)) Immediate memory 77.0 (27.0) Visuospatial/constructional 85.0 (44.5) Language 71.0 (25.0) Attention 62.0 (8.0) Delayed memory 71.0 (16.5) Total scale 62.0 (17.0) APOEe4-negative MMSE at 13 months (median (IQR)) Total 26.0 (8.0) Orientation for time 5.0 (2.0) Orientation for place 5.0 (1.0) APOEe4-positive MMSE (median (IQR)) Total 22.0 (12.3) Orientation for time 2.5 (4.0) Orientation for place 5.0 (1.0)	

	(2.0) Orientation for place 5.0 (2.0)		
Toole 2004[9]	NOT REPORTED	NOT REPORTED	Participants with a history of stroke (model 0: adjusted for 3MS) had an annualised loss of 1.6 (95% confidence interval -2.1, -1.1) points per year more than those without previous stroke. Participants with baseline stroke (model 1: adjusted for prior 3MS, age, sex, race, education, income, smoking, hypertension, antihypertensive and antidepressant medication use, prior diabetes and prior coronary heart disease) had an average 3MS decline of 1.2 (95% confidence interval [CI]: 0.7- 1.7) points per year more than those without one. Results demonstrate that the rate of cognitive decline after ischemic stroke is more than double that of individuals without one. In addition, a recent left hemisphere stroke causes decline 10 times as great as that experienced by persons without one and 60% more rapid than that of persons with a recent stroke in the right hemisphere.
Rowan 2007[11]	Total group CAMCOG 86.6 (7.9) Executive function 14.7 (4.6) Language expression 16.9 (2.0) Power of attention 1.8 (0.7) Total CAMCOG at 3 months post-stroke, study group by quartile homocysteine level Lowest 86.6 (8.3) 2nd 86.5 (8.1) 3rd 87.8 (8.3) Highest 85.7 (6.6) Executive function at 3 months post-stroke, study group by quartile homocysteine level Lowest 15.1 (15.1)	Total group (mean changes (SD) between 3 and 27 months post stroke) CAMCOG -0.6 (7.8) Executive function -2.1 (4.7) Language expression -0.4 (1.8) Power of attention 0.1 (0.4) Total CAMCOG (mean changes (SD) between 3 and 27 months post stroke) Lowest -2.3 (8.4) 2nd 1.1 (8.4) 3rd -0.2 (6.8) Highest -1.7 (7.4) Executive function (mean changes (SD) between 3 and 27 months post stroke) Lowest -2.6 (4.3) 2nd -2.3 (5.9) 3rd -1.5 (3.6) Highest -1.7 (4.5) Language expression (mean changes (SD) between 3 and 27 months post stroke)	51% of elderly non-demented stroke patients have hyperhomocysteinaemia at 3 months post stroke. 79% of elderly stroke patients scored above 80 points on the CAMCOG at 27 months post stroke. Found no associations between homocysteine levels and cognitive change, therefore 3 month post-stroke homocysteine measurement may not predict cognitive decline

	2nd 14.1 (5.3) 3rd 15.0 (4.4) Highest 14.5 (3.6) <u>Language expression at 3 months post-stroke, study group by quartile homocysteine level</u> Lowest 17.1 (2.0) 2nd 16.9 (2.2) 3rd 17.2 (1.6) Highest 16.6 (2.0) <u>Power of Attention at 3 months post-stroke, study group by quartile homocysteine level</u> Lowest 1.7 (0.5) 2nd 1.8 (0.7) 3rd 1.7 (0.5) Highest 1.9 (0.9)	Lowest -0.5 (1.7) 2nd -0.3 (1.9) 3rd -0.2 (2.0) Highest -0.5 (1.4) <u>Power of Attention (mean changes (SD) between 3 and 27 months post stroke)</u> Lowest 0.1 (0.4) 2nd 0.1 (0.6) 3rd 0.1 (0.4) Highest 0.0 (0.3)	

Abbreviations

3MS, modified mini mental; 3MSE, modified mini mental examination; ACS, acute coronary syndrome; ACT, Alphabet Coding Task; ADL, activities of daily living; aMCI, amnestic mild cognitive impairment; AVLT, Auditory Verbal Learning Test; BMI, body mass index; BMSE, Bengali versions of the Mini Mental State Examination; CAMCOG-R, Cambridge Cognitive Assessment; Cambridge Cognitive Assessment (Revised); CES-D, Center for Epidemiologic Study-Depression; CI, Confidence interval; EF, Total executive functioning subtests of the CAMCOG-R (fluency + similarities+ ideational fluency + visual reasoning); CERAD, Consortium to Establish a Register for Alzheimer's Disease; EX, New executive functioning tests (ideational fluency + visual reasoning); FIM, functional independence measure; GDS, Geriatric Depression Score; IQCODE, Informant questionnaire on Cognitive Decline in the Elderly; IQR, interquartile range; LACS, Lacunar stroke; MCI, mild cognitive impairment; MMSE, Mini Mental State Examination; MoCA, Montreal Cognitive Assessment; OCSP, The Oxfordshire Community Stroke Project; OR, odds ratio; PACS, Partial anterior circulation stroke; POCS, Posterior circulation stroke; Repeatable Battery for the Assessment of Neuropsychological Stats (RBANS); RCPM, Raven's Colored Progressive Matrices; SD, Standard Deviation; SE, standard error; SFE, social functioning exam; TACS, Total anterior circulation stroke; TIA, transient ischaemic attack; TUG, Timed Up and Go

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Longitudinal Effect of Stroke on Cognition: A Systematic Review

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3.2.1 PP1 Commentary

In this systematic review (Tang et al., 2018a) we found that although the risk of cognitive decline is increased, cognitive outcome over time is variable. The majority of the studies reported cognitive deterioration over time but there was also cognitive stability and cognitive improvement. However, it is important to note that factors such as follow-up time and the cognitive domain/test being assessed was a factor as to what the cognitive outcome would be over time. These changes in cognitive trajectory are not unexpected as the linear rate of cognitive change seen in the normal aging population is not always seen in the context of stroke (Mijajlovic et al., 2017). This may in part be due to varying degrees of baseline cognition pre-stroke and changes to the rate of decline due to further insult (Mijajlovic et al., 2017). Intact cognition is vital to maintain independence and to be able to carry out activities of daily living. Identifying patterns of cognitive deficit and expected trajectory becomes important not just in the post-stroke rehabilitation phase but also post-stroke recovery.

When looking at global cognitive function, significant decline was found in those who were followed-up over a longer period. Certainly when compared to non-stroke controls, incident stroke has been found to lead to both acute cognitive decline but then also persistent cognitive decline over six years (Levine et al., 2015a). When stroke-survivors are followed-up for even longer, 30% of survivors screen positively for cognitive impairment at 15 years (Crichton et al., 2016). Cognitive batteries looking at global cognition will be important to determine whether individuals should be assessed further for a dementia illness. However, stroke patients will also develop cognitive impairment with deficits in specific cognitive domains without it leading to clinical dementia. In fact in the first year post-stroke 4 in 10 patients will develop cognitive impairment that does not meet the criteria for dementia but may require intervention (Sexton et al., 2019). These specific domains could be targeted by specific clinical groups e.g. speech and language therapy for language impairments or occupational therapists for issues with neglect. Similar to global cognitive function, the effects of stroke longitudinally on specific domains were mixed. There were improvements in some domains such as memory (delayed) (Wagle et al., 2010) at shorter follow-up times, but then decline in others (Comijs et al., 2009, Reitz et al., 2006) when there was longer follow-up, but not universally so. Findings in other domains such as executive function, visuospatial/constructional performance,

information processing and language, were also generally mixed (Tang et al., 2018a). From the point of view of the patient, subjective cognitive complaints are common following a stroke and they tend to increase over time (van Rijsbergen et al., 2014). However, in some studies it has been found that objective cognitive performance does not always independently predict cognitive complaint (Duits et al., 2008) but memory difficulty is among the most frequently reported complaints (Lamb et al., 2013). When assessing the association between these subjective cognitive complaints and objective cognitive performances, the highest correlation was found on the memory domain (van Rijsbergen et al., 2014). A recent study also found that the association between objective cognitive performance and self-reported cognitive complaints 3 months post-stroke was found when a global assessment of objective cognitive performance was done (van Rijsbergen et al., 2017). Again, the strongest domain-specific associations between objective cognitive performance and subjective cognitive complaints was found when ecological tests in the memory domain are used (van Rijsbergen et al., 2017).

Although objective cognitive decline may not always equate to poorer functional performance, it is important to be able to screen for these impairments as cognitive impairment is both prevalent post-stroke even with successful clinical recovery and also related to poor functional outcome (Jokinen et al., 2015). Memory complaints in particular are frequently reported by stroke patients. A recent large survey by the Stroke Association found that 83% of stroke patients have problems with their memory (Stroke Association, 2018a). There is some evidence that memory rehabilitation in stroke patients can help subjective memory problems in the short term but not significantly so in the long term (das Nair et al., 2016). Again this was not evident on objective memory testing (das Nair et al., 2016). A more recent systematic review however did find that psychological interventions may be effective to improve overall post-stroke cognitive function with memory and attention found to have greater benefit than other cognitive domains although the evidence was of poor quality and high risk of bias (Merriman et al., 2019).

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The choice of screening tools may be an important reason for this variability as well as other heterogeneities in design across studies. The studies in this systematic review used traditional cognitive test batteries such as the MMSE. However, stroke-specific screening tools were missing in our review. Stroke specific cognitive screening tools such as the OCS (Demeyere et al., 2015) and the Cognitive

Assessment Scale for Stroke Patients (CASP) (Barnay et al., 2014) have yet to be assessed in any longitudinal studies. This is despite the fact that when compared to the MMSE and MoCA, the CASP has been found to more feasible that the MMSE and MoCA in aphasic stroke patients as it takes into account patients with severe expressive aphasia by using visual items (Benaim et al., 2015, Barnay et al., 2014). Further, the OCS is able to detect a higher incidence of cognitive impairment in stroke patients when compared with the MMSE (Mancuso et al., 2018). When the OCS was compared to the MoCA, the OCS was able to detect significant numbers of patients with cognitive deficits (e.g. neglect, apraxia, number processing) that were undetected when using the MoCA (Demeyere et al., 2016). A substantial number of studies continue to report longitudinal cognitive outcomes but uniformity in, and standardisation of reporting outcomes are needed (Saa et al., 2019). Further, subtle deficits or changes in cognition may therefore not be detected using these other batteries and future studies should look to see if stroke-specific tools are able to assess the true nature of longitudinal cognitive trajectory. These tools will also allow for greater inclusion as they tend to enable the inclusion of those with aphasia and neglect. Universal inclusion should not be at the expense at reduced accuracy however and so care must be taken when comparing those with and without these deficits.

Finally, we also assessed factors that may be related to cognitive decline over time. This included demographic factors, such as age and sex, as well as depression, poorer baseline cognitive test scores and stroke-specific factors such as stroke location (Tang et al., 2018a), which are well known. Other studies have also found associations for progressive cognitive decline in those with other co-morbidities (coronary artery disease (Mahon et al., 2017), arrhythmia (including atrial fibrillation (Mahon et al., 2017, Tang et al., 2006), diabetes (Liman et al., 2011, Jacquin et al., 2014, Wang et al., 2018), leg paralysis (Arba et al., 2017)) and social status (not in a relationship and unemployed (Mahon et al., 2017)). The ever-increasing numbers of risk variables makes it hard to know where interventions should focus on to reduce incident cognitive impairment and dementia. A better way to quantify this risk may be to use a risk assessment approach. Combining risk factors known to increase risk could allow clinicians to target specific populations of post-stroke individuals either for further cognitive assessments following initial cognitive screening or for targeted intervention.

3.3 Chapter Summary

Post-stroke cognitive outcomes can vary as demonstrated across the studies included in this systematic review. This will be down in part to study heterogeneity and the cognitive tests used. However, cognitive trajectory post-stroke does not seem to be a linear process as compared to the general population. Incident stroke may itself accelerate a pre-existing cognitive deficit to the point of a dementia illness or may lead to transient changes in cognition. Better tools and assessment methods are needed so that clinicians are able to identify those at the greatest risk of progression.

Chapter 4: What is the impact of memory deficits on stroke-survivors?

This chapter presents findings from the qualitative interviews conducted with particular focus on how memory difficulties have affected stroke survivors. It is important to understand that although physical recovery may occur for some, we need to understand the impact of the cognitive issues that patients may also experience. Often, these invisible disabilities are hidden from clinicians and service providers. This may be because patients and their families struggle to identify the appropriate service to pursue and are therefore left feeling unsupported in the community.

4.1 Quality of Life After Stroke

Globally, the lifetime risk of stroke from the age of 25 is around 25% for both men and women (Feigin et al., 2018). In 2016 there was an estimated 80 million stroke-survivors (GBD 2016 Stroke Collaborators, 2019). Stroke is therefore a leading cause for mortality and disability with substantial associated economic costs (Rajsic et al., 2019, GBD 2016 Stroke Collaborators, 2019). Returning home to familiar environments having had a stroke can be challenging. For many, once they are home, patients can experience a deep change in their lives and they can also feel that they were now also a burden on their families (Simeone et al., 2015). Particularly as almost half of stroke-survivors living in the community require a caregiver at home to help them with post-stroke sequelae (Mayo et al., 2002). Further, relationships with a partner and family can also be negatively affected (McKevitt et al., 2011). As much of the informal care tends to be provided by family and partners (Greenwood et al., 2008), this places a significant degree of burden on these individuals. Treatment burden, defined as the amount of work of healthcare for patients (Eton et al., 2012), is also significantly influenced by the configuration of both health and social care (Gallacher et al., 2018). Examples of treatment burden include the fact that patients need to make sense of stroke and planning care, needing to interact with others e.g. their family doctor, family members and allied health professionals and being able to carry out management strategies (Gallacher et al., 2018). So, we can see that not only does the stroke-survivor need to be able to manage any post-stroke sequelae, but they also have to learn to adjust to new environments and changes in roles and relationships.

Rachpukdee and colleagues have also found that a predictor of unsatisfactory quality of life was severe cognitive impairment (Rachpukdee et al., 2013). Even following a TIA or minor stroke, patients and healthcare professionals recognise the impact of cognitive impairment (Turner et al., 2019). At the more severe end of the spectrum, dementia following a stroke can remain undetected. In the community, it has been estimated that over 60% of cases of dementia were undetected (Lang et al., 2017). Amongst a number of factors, low priority to discuss cognitive impairment with a physician, assuming that these changes are part of normal aging as well as fears around dementia all contribute to a missed or delayed diagnosis of dementia from the patient's perspective (Bradford et al., 2009). This means that it would be extremely difficult for primary care clinicians to be able to pick up those that need the additional support, intervention and onward referral to memory clinic services to obtain a diagnosis of dementia. It is therefore important for clinicians to be aware of how cognitive changes such as memory problems are affecting stroke survivors on a day to day basis to help them recognise those that require additional attention.

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4.2 PP2. Impact of Memory Problems Post-Stroke on Patients and their Family carers

Tang EYH, Price C, Stephan BCM, Robinson L, Exley C. (Frontiers in Medicine); 2020; 7: 267 (Invited to participate as part of "Dementia in Primary Care" collection)

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Impact of Memory Problems Post-stroke on Patients and Their Family Carers: A Qualitative Study

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Background: Memory problems post-stroke are common and for some, these problems could then progress to a dementia illness. Once in the community, stroke-survivors are looked after by their family doctors although there is evidence that these patients may struggle to access appropriate help in the community for these problems. Although a stroke-survivor may be physically capable of performing daily tasks, they and their families may have to learn to manage and adapt to their new memory deficits. There is often less focus on cognitive recovery post-stroke from clinical services perhaps because of the lack of awareness and evidence of these adaptations. There is also good evidence that organized stroke care improves physical recovery but no equivalent evidence for the effectiveness of cognitive rehabilitation. The aim of this qualitative study was to report the impact of memory problems on the stroke-survivor and their family once they are living in the community.

Methods: Semi-structured interviews were conducted with patients and family carers to gain an in-depth understanding of their experiences. Participants were invited to take part in an interview at around six and 12-months post-stroke. A topic guide was developed to explore participant's care experiences post-stroke when they have also presented with memory difficulties. Data collection and analysis were iterative; all transcripts were anonymized. The data were thematically analyzed.

Results: Twenty-two interviews were conducted. Five family carers and ten stroke-survivors were interviewed at six-months post-stroke, of these eight stroke-survivors and four family carers agreed to a 12-month follow-up interview. They identified several areas of impact: (1) impact on daily life; (2) emotional impact; and (3) compensating strategies implemented in response to impact.

Conclusion: Living with stroke combined with memory impairment can have negative effects on the stroke-survivor and their family once in the community. Health professionals and services in the community need to recognize the burden of managing symptoms post-stroke for these individuals and their families. Understanding the impact can enable more effective community and specialist support to be provided particularly if we were to also identify those who may then be at risk of a future dementia illness.

Keywords: stroke, cognition, qualitative, primary care, dementia

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INTRODUCTION

Following a stroke and discharge from specialist services into the community, patients are expected to navigate through complex health systems and treatment regimens whilst recovering (1). However recovery in the community involves not only dealing with physical aspects, but the psychological and emotional impact of the stroke, to enable the individual to rebuild and restructure their world (2). For some stroke-survivors the "unseen" emotional changes post-stroke can be more disabling than the physical impairments (3).

Post-stroke cognitive deficits are common (4) and add to the challenges already faced by stroke-survivors. In terms of current services, primary and secondary healthcare professionals have already identified a lack of clarity when managing stroke individuals with memory difficulties (5). Similarly, patients provide accounts of fragmented care (1), which could have a negative impact on the stroke-survivor and their families. Although there have been calls for stroke clinicians to have increased awareness of the cognitive consequences of stroke (6), even if this happens, services presently available to support patients and families are limited. A previous survey by the Stroke Association found that 77% of stroke survivors have problems with memory yet nearly 50% of stroke-survivors reported that the support they received for their memory problems and fatigue was poor (7). The recent NHS Long Term Plan has specifically highlighted the need for stroke rehabilitation, which is better integrated into community care for the longer term (8). In order for this to be achieved, there needs to be greater awareness of post-stroke cognitive changes particularly in primary care where these patients will be discharged to.

Stroke is known to be a strong independent risk factor for dementia (9). In fact, around 10% of individuals will develop dementia soon after their first stroke and around a third will be affected after recurrent stroke (10). Compared to the general population, the incidence of dementia is nearly 50 times higher in the year after a major stroke (11). However, it is clear that for those with memory problems post-stroke, they have obstacles in accessing primary healthcare services (12). A recent systematic review has highlighted the dissatisfaction amongst stroke-survivors and caregivers with the lack of proactive follow-up, which includes primary care (13). It is not only marginalization that leads to this sense of abandonment but these patients also do not have the skills to re-engage with services (13). It has become increasingly apparent that the role of primary care is to provide this continuity of care for these patients, particularly if we also wish to identify those at the greatest risk of developing a future dementia illness. Highlighting the "hidden" impact of reduced cognitive performance following stroke could assist clinicians in understanding the variation in difficulties experienced and recognizing when additional assessment might be necessary.

To assess whether there is a need for additional services following discharge into the community, it is necessary to describe and highlight the daily impact of cognitive impairment post-stroke. The aim of these qualitative interviews was to seek understanding of the scale and nature of impact of memory problems for stroke-survivors and their families in the community.

METHODS

Design and Setting

Qualitative semi-structured interviews were conducted with community dwelling stroke-survivors and their family carers from the North-East of England. Older stroke-survivors (aged over 60 years old) who presented to their six month post-stroke specialist review and expressed any subjective memory concern following their stroke were invited to participate in the study. If applicable, their family carers were also invited to participate. If people were interested in taking part, their contact details were passed onto the research team. Purposive sampling was used to ensure that a range of experiences could be captured i.e. to ensure a mix of genders and a range of carers were recruited. One researcher, a medical doctor (EYHT), then contacted the individual to provide further information regarding the study and provide an opportunity for potential participants to ask questions. If they agreed, participants were asked to take part in an interview soon after their six-month stroke clinic review (baseline) or around 12 months post-stroke (follow-up) or at both time points.

Data Collection

Semi-structured interviews were used to elicit the experiences of stroke-survivors who subsequently developed memory problems. Following a review of the literature and discussion amongst the research team an interview topic guide was created. Interviews were designed to seek participants' views on a range of topics including their experiences in stroke services, their subsequent experiences of living in the community e.g., in seeking support and information if their memory did not improve and their feeling toward risk assessment for dementia. This paper focuses on the impact of memory problems after stroke, which participants elaborated on when discussing these main topics. Other topics in this study including access to services (12) and views on risk assessment for dementia have been published separately (14). The study took an iterative approach. That is, data collection and analysis occurred concurrently, to ensure that emerging topics identified in earlier interviews could be explored in subsequent ones. Interviews were conducted between April 2016 and August 2017 in participants' place of choice (their homes) either individually or together if requested by both participants (i.e., stroke-survivor and family carer together).

Data Analysis

All interviews were digitally audio recorded, anonymized, and transcribed verbatim. Data analysis followed the principles of the constant comparative method (15) and the data was thematically analyzed (16). One researcher (EYHT) familiarized himself with all interviews and read all transcripts line by line and coded the data to identify some initial themes. Two members of the team (EYHT and CE) went through these themes to identify areas of overlap. These themes were subsequently categorized into broader overarching themes to provide an

TABLE 1 | Interview participants.

Unique identifier (patients and carers)	Role	Gender	Age	Ethnicity	Follow-up interview
P1	Stroke-survivor	Female	80	Caucasian	No
P2	Stroke-survivor	Female	76	Caucasian	Yes
P3	Stroke-survivor	Female	72	Caucasian	Yes
P4	Stroke-survivor	Male	75	Caucasian	Yes
P5	Stroke-survivor	Male	80	Caucasian	Yes
P6	Stroke-survivor	Male	74	Caucasian	Yes
P7	Stroke-survivor	Female	73	Caucasian	Yes
P8	Stroke-survivor	Female	82	Caucasian	Yes
P9	Stroke-survivor	Male	84	Caucasian	No
P10	Stroke-survivor	Male	79	Caucasian	Yes
C1	Carer of P1 (Husband)	Male	79	Caucasian	No
C2	Carer of P4 (Wife)	Female	79	Caucasian	Yes
C3	Carer of P5 (Daughter)	Female	57	Caucasian	Yes
C4	Carer of P6 (Wife)	Female	71	Caucasian	Yes
C5	Carer of P8 (Daughter)	Female	60	Caucasian	Yes

overview of participant views. Data collection ceased when data saturation had occurred, which was defined as the point where informational redundancy had been reached (17). These themes were discussed and agreed with the wider researcher team. The data was managed on NVivo 11 software. The paper conforms to the Standards for Reporting Qualitative Research checklist (18) (**Supplementary Table 1**).

RESULTS

Twenty-two interviews were conducted in total. Ten stroke-survivors and five carers were interviewed at 6 months post-stroke, of these, a further eight stroke-survivors and four carers agreed to an interview 6 months later (see **Table 1**). During interviews, participants discussed in detail the impact of their memory problems following their stroke and these have been grouped into three themes.

Impact on Daily Life

Stroke-survivors and their carers were asked directly how their lives had been affected by their new memory difficulties following their stroke. Stroke-survivors gave examples of general everyday activities which they had started to struggle with. This ranged from remembering important dates to doing everyday tasks both at baseline and follow-up interviews:

> *"…I think it's getting worse. I had a bad day yesterday. I really felt- I call bingo at the over 60s and I've been doing it for five year and yesterday, I couldn't remember how to use the machine. I didn't switch it on right and I had to get someone to come and reset it. I just couldn't remember." (P3 at baseline)*

> *"It's funny. I've got a car, and I had a puncture, and it was funny and I knew I had a puncture, and yet when I hopped into the car the following days, and I was driving along the road, "Oh, God. I had a puncture" … I had to stop the car and see it was still flat." (P10 at follow-up)*

In addition to discussing how everyday activities were affected, stroke-survivors often commented on the difficulties they had during conversations with others:

> *"I can be in the middle of a sentence and I forget what I'm talking about, I've really got to sit and think. Emm, I can go to the shops and I'll be in the shop … I want something and when I want something but I can't think of exactly what I want. I can show them, but I cannot tell them." (P7 at baseline)*

For this participant the conversational difficulties were still apparent at her follow-up interview:

> *"Trying to make conversations at times is very hard and I get my words mixed up or I can't say them … I know they're there, but I just can't get them out, emm but the people that are around us all knows and they'll put us right, or I'll look at them and say, "What was that again?" … I'm in the middle of a conversation and then me mind just completely goes blank now. "What was I saying?" As soon as they put us right, I can pick the conversation up again as such, or I'll keep repeating myself." (P7 at follow-up)*

It was also quite clear to family members caring for the stroke-survivor what a significant impact the memory problems had become for the individual:

> *"… Taking him outside, as soon as he went out the front door, he got used to being in the house and he knew where he was in the house. Got him to the front door and he was just stopped and looking in the street. He didn't recognize the street. Emm and even when we came back he would continue walking past the house. Didn't realize he'd got home. Emm, that has improved … He's going round the block, round the estate his self sometimes." (C3 at baseline)*

Emotional Impact

Both stroke-survivors and their family carers reported examples of how their memory difficulties affected them emotionally. Stroke-survivors were finding their need to rely and loss of independence hard as this represented a significant change in role and challenge to their own identity:

> *"It's the depending on people, which I didn't used to. I was the one that people came and said," Dad, have you got time for to do this or do that. "Now I'm depending on them, that's, that's the part I'm finding hard." (P5 at baseline)*

This may lead to low confidence in being able to deal with activities they would attribute to their pre-stroke selves:

> *"I'm slowly getting that back; I've got bits of memory back but I haven't got sufficient to – because I've been asked to take back me chairmanship and really I'm not confident enough to do it." (P4 at baseline)*

Carers commented on the frustration when the stroke-survivor would forget to do simple tasks:

> *"Oh yeah well, I mean he doesn't seem to retain it. When I tell him something he can't retain it and I suppose if you can't take it in, you can't remember it. So that's a problem and I get frustrated sometimes and I get angry with me self for getting frustrated because I know he can't help it … [Stroke-survivor] always put like the bins out and when they were done then he would come bring them in and things like that and now I went out the other night and he hadn't brought them in and I thought, "Oh for goodness sake."" (C4 at baseline)*

For some carers it was frustrating that the stroke-survivor seemed oblivious to the their efforts in looking after them:

> *"But I have lost my temper with her a couple of times, and I have actually shouted at her and said, "You cannot do this … it's not safe for you, you cannot do it. You've got to listen and do as you're told." She doesn't take it very easily, and the next morning she forgot it's ever happened … Then I didn't feel good, I felt terrible doing it." (C5 at baseline)*

Families of stroke-survivors were also concerned about undermining or hurting the feelings of the stroke-survivor as they tried to deal with the difficulties encountered:

> *"…He still asks the same question two or three times. Even though you've said, "We've already told you that." And the hardest part is with wur family, because they're having to say, "We've already heard that." Or, "You've already asked [me] that." And they are feeling a little bit disrespectful, if you understand what I mean? (C2 at follow-up)*

However, interviews at 12-months, suggest that for some family members they had felt that things had changed for the better as there was more acceptance of the new normal:

> *"But as I say, he seems to be like laughing about it more. Whereas before it was like, really, he was getting uptight about, "Oh, here we go again, I've done something stupid. I've said something stupid. I know I've said this umpteen times." But now he takes it more sort of in his stride." (C3 at follow-up)*

Compensating Strategies Implemented in Response to Impact

Responding to their new memory difficulties, stroke-survivors would often adapt and find new practical ways to manage their symptoms in order to appear to function 'normally' in the community.

> *"If I'm going anywhere like that, I'd always try to arrange to put the money, if I'm like we get a taxi, now I put the money in this pocket for me taxi so I know that I've got it there. And that's what I do, I put things like ready for us just to pay out and it's not as much distraction to meself" (P1 at baseline)*

Participants would discuss the need to find ways of reminding themselves of everyday activities:

> *"Like, I had an appointment for the vet for the dog and because I didn't look at the notice board, I nearly forgot it. I had to get, rush at the last minute to the vet. Eh, so, now, before I go to bed, I sit with a piece of paper and I write down the things I have to do the next day. Emm, me friend have- me and Lavender spend a lot of time together and if she's coming, or I'm supposed to go there, I always have to ring and ask her again, "What time are we going to meet?" Because I forget." (P3 at baseline)*

Writing things down and preparation were common methods used by stroke-survivors to help them remember. This was important both to enable them to continue to function and participate in their community:

> *"I don't like to do, mess anybody around like you know. What I'm doing now is I've got a calendar behind you, I write everything- every, try to write everything down now like you know so I don't forget. And em it was funny because em I had some more, I had some tests just before Christmas because our doctors, it's just local, start changing medication. And oh gosh, and with it being the end of the year and I hadn't got- Funnily enough, I didn't have a new calendar for to put the new ones on. And ey the things I was forgetting, I went- Actually I went and saw the chemist and em she em put me on the right road like you know, and different things. Even the chemist phoned me up to see how I was getting on with me medication like you know." (P10 at baseline)*

At follow-up the same participant discussed further adaptations that he made as time had passed. These adaptations were necessary so that he would remain up to date with current events and relevant in his social circle:

> *"Respondent: … but if I put the television on or I read the paper, and I read about things … now I'll go out tonight. On a Friday, I only go out on a Friday and Saturday night, you know just to have bit chinwag with me friends at the local club … I'll show you. I write it all down, most of it down and em what's going on in the football world, you know? And I write it down and I digest this before I go out tonight. ….so, I know what I'm talking about. ….. Because we're talking about stuff I don't know anything about. I've missed it, you know? And I says oh I missed this, that… I don't like to be, what's the word? Pushed out, because I don't know what I'm talking about, you know." (P10 at follow-up).*

Carers also gave examples of how they also needed to adapt in terms of changing roles and the impact on their lives:

> *"There's a complete role reversal now. I am the carer and she's now the dependant. Any medical visits, any visits to the doctors, any organization of prescriptions, anything like that I have to do." (C5 at baseline)*

Stroke-survivors themselves also recognized the significant role their family played in their ongoing care and support:

> *"I often thought, you know someone who hasn't got this, these people [family] around ya and everything, it must be very hard." (P4 at baseline)*

"You see, I said the other day, "I don't think I've seen my own doctor," and she says, "Mum, she's been twice to see you." Well, I've, I've forgotten. I can't remember that, and she says she's been twice and she says I've only got to pick up the phone and tell her and she'll be here." (P8 at baseline)

However, one family carer participant remarked that although she was now undertaking more tasks which many would associated with being a more formal caring role, she did not see herself as a carer and she was still very much a spouse first and foremost:

"One of our friends suggested that I put in for a carer's allowance and then I thought, I thought I don't want to be a carer, I'm not his carer, I'm his wife. You know, I mean wives help their husbands, like husbands help wives don't they. I thought no I'm not doing that, no, no, no." (C4 at baseline)

DISCUSSION

In this study, we have been able to describe the impact of post-stroke memory problems on the stroke-survivor and their families once they are in the community. The impact can be practical or emotional, and lead to changes and adaptations in order for the stroke-survivor to continue to function in the community. Participants have mainly described compensating strategies without the input from a healthcare professional. This may mean that these deficits are invisible to their family doctors or multidiscplinary rehabilitation teams. There may also be a lack of appropriate mechanisms or pathways by which clinicians are able to recognize and support these individuals, who then took their own actions to try to reduce the impact of their cognitive difficulties. For some, these deficits persist and primary care clinicians should be aware of the longer term affects of such cognitive difficulties even when other more visible physical deficits have improved. This would enable clinicians to advise patients and their families so that they can ensure long-term support is available when necessary without the need for additional carer burden.

A recent meta-analysis found that the pooled prevalence of those with cognitive impairment one year post-stroke was 38% (19), but this may not necessarily be due to the most recent cerebrovascular event. Indeed, cognitive problems may instead reflect new identification of problems with non-stroke causes present amongst older people. For many, cognitive dysfunction may still be present even when there are minimal or no physical disabilities (20). In a study looking at domain-specific cognitive impairments 3 months following a stroke, it was found that even in cases with excellent clinical recovery (modified Rankin Scale = 0–1, no disability) 71% of participants had some cognitive impairment (21). Further, at 15-month follow-up domain-specific cognitive impairments were related to functional disability (21). There are also interactions between cognitive and mental health as perceived stress and depressive symptoms could also increase the likelihood of having subjective cognitive complaints (22). Participants in this study demonstrated the physical and emotional impact that the stroke and additional memory problems have had on their daily lives. Living with a potentially disabling chronic condition such as stroke, in addition to new cognitive deficits adds additional burden to the stroke-survivor and their families. Indeed, subjective cognitive complaints (with working memory being the most frequent) have been shown to predict difficulties with social intergration but can be mediated by depressive symptoms (23). Further, objective cognitive test performance has been found to be associated with self-reported cognitive complaints with the strongest association being found in memory (24). However, this is not always necessarily the case for example in young stroke patients (25) where cognitive metrics are less well developed or when the perceived cognitive difficulty is a reflection of psychological distress and low mood (26).

Although cognitive outcome following a stroke can vary (27), there is the risk of progression to post-stroke dementia (4). It is therefore important to be able to have systems in place to ensure these individuals receive adequate support particularly as subjective memory complaints can predict 2-year incident dementia (28). The period following their stroke and then possible transition to long-term cognitive failure or even a dementia illness itself can be extremely difficult for the stroke-survivor and their families. Looking at the dementia diagnostic journey in general, a core feature running through is in fact "living with uncertainty" (29). Outwith the context of stroke, the time from thinking something may be amiss to then looking to make contact with a healthcare professional can be as long as two and a half years for dementia (30). However, this transition to illness recognition to illness presentation is not confined to dementia alone (29) and will be applicable to stroke-survivors dealing with their post-stroke selves. Therefore stroke-survivors with memory difficulties will not only have to live with the uncertainty of their stroke but may also have to live with the uncertainty of a potential dementia illness. Even if they do not develop dementia, many of them will still need to live with persisting cognitive deficits and healthcare professionals and services need to be able to recognize the additional burden this presents to the stroke-survivor and their families.

Many stroke-survivors report unmet clinical and social needs following their stroke (31). Further, stroke-survivors and their caregivers can feel abandoned due to for example passivity of services or perhaps because they do not have the knowledge or skills to re-engage (13). Yet patients and their families still need to find ways to adapt in order to continue to function in the community. Looking to adapt to their new difficulties was found to be important in a number of ways for both sets of participants in this study. In particular, as one post-stroke participant reported, there was the need to feel that they remain relevant and not excluded in their social circles. Indeed, regaining their social and community activities following a stroke can confer a sense of confidence and connection to family and friends (32). However, previous research has also found that, when discussing quality of life, stroke-survivors often discussed changes in social relationships for example feelings of frustration from increased dependence on others (33). Similarly, "carers" interviewed for this study were family carers or informal carers i.e., they may not recognize themselves as a carer. Previous research has highlighted the importance of informal carers in the management of long term conditions (34), and also that

spouse carers of individuals with other chronic conditions, such as multiple sclerosis, resist both the role and the label of a carer (35). Family carers in this study often carried out caring duties not because of any formal perceived change in role but because of their pre-existing relationship with the stroke-survivor. They did not see it as a requirement, rather a natural part of a reciprocal relationship. However, resisting the identity of a carer could mean that they are also less likely to acknowledge the need for support (36). Health professionals need to recognize that in order to enable and support a stroke-survivors social network, besides accounting for the possible impact of both physical and language disabilities, changing social needs should also be recognized (37). Primary care professionals who may have pre-existing relationship with these individuals are well placed to provide such holistic assessments and care.

The hidden impact of subjective memory deficits is not insignificant as evidenced by the fact that participants in this study had themselves often adapted according to individual circumstances. The role of primary care clinicians could be to follow-up these patients more readily post discharge from specialist stroke services with onward referral to the appropriate service. This could be tackled in two ways. First, referral for formal assessments of cognition and intervention through psychological services or memory clinic referral if applicable, second, practical assistance to support patients to continue to live well and safely in the community. However, if more formal psychological intervention for example cognitive rehabilitation is to be offered, then these services need to be made more readily available in the community. In England, neuropsychology assessment after stroke to assess cognitive difficulties and provide support is often not formally available (38). From a practical point of view, patients could also be referred to community allied health professionals for assessments and continued adaptive interventions, for example occupational therapists to enable them to adapt and manage better in their own homes. To facilitate this, there needs to be agreement and consensus across different hospital and community services about the pathway specific for this group of individuals with relevant information and practitioner training available to assist clinicians.

Strengths and Limitations

There are several strengths to this study. We were able to capture the experiences of stroke-survivors and their families over time when adapting to their new memory problems following discharge from stroke specialist services. We do recognize some limitations. We confined the study to one area of England (i.e., the North-East) and the study participants were all Caucasian. However, services post-stroke will be similar across England and we would anticipate the experiences of others exhibiting memory deficits post-stroke would be similar. Further studies should look to assess whether there are any cultural aspects which may impact upon these individuals in addition to what has been found in this study, particularly amongst informal family carers in other ethnicities. We also recognize that we have only recruited participants who had memory deficits and other cognitive (e.g., visuospatial, attention etc) deficits have not been included. We recruited participants from stroke clinics and cognitive assessments were not performed. This meant that we could only assess those who self-reported memory disturbance as other cognitive domains were not tested for. Finally, we recognize that we only had female family carers in this study, which reflects the nature of the stroke population. As such, we are not able to elaborate whether the same issues would be found in male family carers.

CONCLUSION

The addition of a cognitive problem such as memory difficulties can add significant burden to both the stroke-survivor and also their family carers. There is evidence from this study that when participant's were followed up, they do manage to compensate. This compensation often involves the family which can result in additional burden on the family carers who may not identify themselves as carers in the first place. Clinicians need to be aware that these invisible aspects of stroke can persist and that stroke-survivors and their family may require additional post-discharge support in the community. However, timely support can only be offered in the community if the appropriate services and pathways are also available to the primary care clinician. Showing evidence of need is the first step toward developing that care provision.

DATA AVAILABILITY STATEMENT

The datasets for this manuscript are not publicly available because the data are transcripts of interviews that reflect the views of individuals and complete anonymization cannot be guaranteed. Requests to access the datasets should be directed to Eugene Tang, e.y.h.tang@newcastle.ac.uk.

ETHICS STATEMENT

The study involving human participants was reviewed and approved by London—Hampstead Research Ethics Committee (reference 16/LO/0133). The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any data included in this article.

AUTHOR CONTRIBUTIONS

ET conceived the framework for this study, collected, analyzed and interpreted the data, and prepared the manuscript for submission. CP helped to conceive the framework for this study and critically evaluated the manuscript. BS helped to conceive the framework for this study and critically evaluated the manuscript. All authors contributed to the article and approved the submitted version. LR helped to conceive the framework for this study and critically evaluated the manuscript. CE helped to conceive the framework for this study and assisted with the analysis of the data and contributed to the drafting of the manuscript and also critically evaluated the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2020.00267/full#supplementary-material

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The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Supplementary Table 1: Standards for Reporting Qualitative Research Checklist[1]

No.	Topic	Item	Page(s)
	Title and abstract		
S1	Title	Concise description of the nature and topic of the study Identifying the study as qualitative or indicating the approach (e.g., ethnography, grounded theory) or data collection methods (e.g., interview, focus group) is recommended	1
S2	Abstract	Summary of key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results, and conclusions	1
	Introduction		
S3	Problem formulation	Description and significance of the problem/phenomenon studied; review of relevant theory and empirical work; problem statement	2
S4	Purpose or research question	Purpose of the study and specific objectives or questions	2
	Methods		
S5	Qualitative approach and research paradigm	Qualitative approach (e.g., ethnography, grounded theory, case study, phenomenology, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g., postpositivist, constructivist/ interpretivist) is also recommended; rationale[b]	2
S6	Researcher characteristics and reflexivity	Researchers' characteristics that may influence the research, including personal attributes, qualifications/experience, relationship with participants, assumptions, and/or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results, and/or transferability	2
S7	Context	Setting/site and salient contextual factors; rationale[b]	2-3
S8	Sampling strategy	How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g., sampling saturation); rationale[b]	2
S9	Ethical issues pertaining to human subjects	Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	2
S10	Data collection methods	Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources/methods, and modification of procedures in response to evolving study findings; rationale[b]	2-3
S11	Data collection instruments and technologies	Description of instruments (e.g., interview guides, questionnaires) and devices (e.g., audio recorders) used for data collection; if/how the instrument(s) changed over the course of the study	2
S12	Units of study	Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	3
S13	Data processing	Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymization/deidentification of excerpts	2-3
S14	Data analysis	Process by which inferences, themes, etc., were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale [b]	2-3
S15	Techniques to enhance trustworthiness	Techniques to enhance trustworthiness and credibility of data analysis (e.g., member checking, audit trail, triangulation); rationale[b]	2-3
	Results/findings		
S16	Synthesis and interpretation	Main findings (e.g., interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	3-5
S17	Links to empirical data	Evidence (e.g., quotes, field notes, text excerpts, photographs) to substantiate analytic findings	3-5
	Discussion		
S18	Integration with prior work, implications, transferability, and contribution(s) to the field	Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application/ generalizability; identification of unique contribution(s) to scholarship in a discipline or field	5-6
S19	Limitations	Trustworthiness and limitations of findings	6
	Other		
S20	Conflicts of interest	Potential sources of influence or perceived influence on study conduct and conclusions; how these were managed	8
S21	Funding	Sources of funding and other support; role of funders in data collection, interpretation, and reporting	7

Reference

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4.2.1 PP2 Commentary

In this paper, themes relating to the impact of stroke and also subsequent memory problems on the patient and their family were analysed. Participants in this study provided examples of difficulties in their daily lives and also the emotional impact of these difficulties. However, they also discussed ways that they would adapt to their new difficulties. These compensatory strategies could mean that they would either delay or even avoid seeing a healthcare professional. This would also mean these deficits remain invisible to healthcare professionals whilst the stroke-survivor and family carers continue to struggle on in the community.

Longer term outcomes can remain poor for stroke-survivors with stroke often seen as another step towards declining health (Hawkins et al., 2017). There also tends to be much emphasis on physical recovery and rehabilitation following a stroke. Patients themselves will focus on the physical issues when discussing overall recovery even if they reported symptoms related to cognition problems such as memory loss deficits which have a negative impact on their lives (Ellis et al., 2013). Specifically cognitive difficulties following a stroke can affect a stroke survivor's recovery (Babulal et al., 2015) and in particular post-stroke physical functioning (Nyunt et al., 2014). In a study looking at domain specific problems encountered by stroke-survivors, nearly all participants reported cognitive changes with no differences across gender or ethnicity (Pappadis et al., 2019). In this study, nearly half of participants reported memory difficulties with examples provided including difficulty in remaining focussed or walking away whilst cooking (Pappadis et al., 2019). Emotional problems following a stroke are known to be a common occurrence (Chen et al., 2019a) which also tends to be less frequently met when compared to other problems such as problems with incontinence, mobility, speaking, reading sight and falls (McKevitt et al., 2011). The emotional impact expressed by participants was within the context of their changing roles due to either lack of confidence or loss of independence.

This study was able to provide more an in-depth account of not only the effect of these memory difficulties but how participants were compensating for these difficulties. In a qualitative meta-synthesis of literature focused on the experience of those living with stroke, similar themes were found although did not look specifically at those living with cognitive changes (Salter et al., 2008). In this synthesis of qualitative studies, a similar theme of "adaptation and reconciliation" was found

representing the stroke-survivor's resilience and ability to make changes to focus on more positive aspects of their lives (Salter et al., 2008). Similarly, a further study looking at the process of adjustment over time post-stroke found that part of this process was termed "evolving a new normal" (Theadom et al., 2019). Over time, participants in this study were not only more aware of their limitations but were able to make adjustments to their life (Theadom et al., 2019), similar to participants in my own study. Adaptations may be perceived as a negative consequence post-stroke. This is because the need to adapt has meant that the individual has needed to perhaps adjust away from their former selves to live with their new post-stroke selves and subsequent disabilities. A systematic review of qualitative studies found that in order for stroke-survivors to adapt and recover, the individual also needs to engage in this process. Engagement in meaningful activities can help the stroke-survivor attain a sense of belonging, purpose and to regain some of the autonomy they may have lost and includes social participation (Lou et al., 2017). This was certainly relevant to one participant in the qualitative study who spoke of purposely doing some learning before meeting up with his social circle so that he could continue to engage with them and remain relevant to his peers (Tang et al., 2020a). Many of these adaptations are often made without the explicit assistance of healthcare professionals. Healthcare professionals themselves may not be aware of the additional "work" that the patient has had to give themselves in order to adapt, engage and recover.

4.3 Chapter Summary

Although previous qualitative studies have looked at the long-term trajectory of recovery post-stroke, this qualitative study has been able to track the trajectory of a specific subcategory of stroke patients i.e. those who are struggling with their memory. In general, the themes are similar to the ones the general stroke population may face. It is clear from these accounts that stroke-survivors with memory problems are able to learn to adjust to their new post-stroke selves. They are able to adapt and make seemingly small changes to continue to function in the community. However, there are undeniable physical and also importantly hidden emotional affects that this can have on the stroke-survivor and their family. Many stroke-survivors with memory problems feel that the support they receive for these problems is poor. It is not clear whether this is because the support available was substandard (or not available) or whether they had just not known how to access this support. It is therefore important

to be able to clarify the stroke survivors' clinical journey from specialist assessment to community discharge under the care of primary care services.

Chapter 5: Views of stakeholders on current care for post-stroke cognitive deficits?

In this chapter, findings from a qualitative interview study with clinicians involved in post-stroke care are presented. This included both primary and secondary care clinicians. The views and experience of stroke-survivors and their family carers were also sought. These interviews were conducted to gain a more in depth understanding of the current clinical service pathway for stroke patients presenting with cognitive difficulties such as memory problems, in order to highlight any issues or gaps in care. The aim of this study was to assist in the development of other approaches to assist clinicians in future service improvements and/or identify questions for future research.

5.1 Clinical Care of Memory Problems Post-Stroke

The potential problems a stroke-survivor may face in the recovery and rehabilitation phase are extensive. Cognitive deficits, such as overall cognitive impairment, difficulties with memory, attention and concentration, executive function and spatial awareness, can all impact on the patient (Rodgers and Price, 2017). The multidisciplinary nature of stroke care ensures that deficits such as these can be addressed via appropriate professional expertise from a range of staff via post-stroke clinical contact with the patient and their families. Memory deficits post-stroke are common even when there has been successful functional recovery (Jokinen et al., 2015). National clinical guidance has recommended therapy to preserve abilities as well as being trained in compensatory techniques e.g. electronic reminders or written checklists (Intercollegiate Stroke Working Party, 2016). This is particularly relevant as specific cognitive domains such as attention and memory have been found to show greater benefit from psychological interventions than other domains (Merriman et al., 2019). There have been repeated calls for clinicians to take a more active role in the area of post-stroke cognition (Lodder, 2007, Pantoni, 2017). At present much post-stroke care and research focuses on physical recovery with cognitive issues often not always addressed. As stroke survival increases in an aging population, the bulk of stroke care may further overwhelm the chronic post-stroke phase. This is particularly important as the biggest increase in stroke care costs is anticipated to be in social care (King et al., 2020). This has led to international consensus recommendations culminating in the Berlin Manifesto which calls for the joint prevention of stroke and dementia (Hachinski et al., 2019).

As an initial step to understand the clinical aspects of this growing problem, it was firstly important to clarify from the clinician's perspective the pathway for managing stroke-survivors with subsequent memory deficits as to whether there may be gaps in care for stroke-survivors with subsequent memory deficits.

5.2 PP3. Gaps in care for patients with memory deficits after stroke: views of healthcare providers

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Tang et al. BMC Health Services Research (2017) 17:634
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RESEARCH ARTICLE Open Access

Gaps in care for patients with memory deficits after stroke: views of healthcare providers

Eugene Yee Hing Tang[1*], Christopher Price[2], Blossom Christa Maree Stephan[1], Louise Robinson[1] and Catherine Exley[3]

Abstract

Background: Stroke is a common cause of physical disability but is also strongly associated with cognitive impairment and a risk for future dementia. Despite national clinical guidelines, the service provided for stroke survivors with cognitive and memory difficulties varies across localities. This study critically evaluated the views of healthcare professionals about barriers and facilitators to their care.

Methods: Seventeen semi-structured individual interviews were conducted by a single interviewer with both primary and secondary care clinicians in regular contact with stroke-survivors. This included stroke medicine specialists, specialist nurses, physiotherapists, occupational therapists, general practitioners and primary care nurses. Topics included individual experiences of the current care offered to patients with cognitive impairment, assessment processes and inter-professional communication. Interviews were audio recorded and transcribed verbatim. Transcripts were thematically analysed and themes grouped into broad categories to facilitate interpretation.

Results: Data analysis identified four key themes as barriers to optimal care for stroke-survivors with memory difficulties: 1) Less focus on memory and cognition in post-stroke care; 2) Difficulties bringing up memory and cognitive problems post-stroke; 3) Lack of clarity in current services; and, 4) Assumptions made by healthcare professionals introducing gaps in care. Facilitators included stronger links between primary and secondary care in addition to information provision at all stages of care.

Conclusions: The care provided by stroke services is dominated by physical impairments. Clinicians are unsure who should take responsibility for follow-up of patients with cognitive problems. This is made even more difficult by the lack of experience in assessment and stigma surrounding potential diagnoses associated with these deficits. Service development should focus on increased cohesiveness between hospital and community care to create a clear care pathway for post-stroke cognitive impairment.

Keywords: Stroke, Memory, Cognition, General practitioners

Background

Stroke is a leading cause of morbidity worldwide and the third most common cause of disability [1]. This is not only a result of effects on motor function but because stroke is also associated with cognitive impairment and an increased risk of dementia [2–4]. Indeed, one in three people will experience stroke, dementia or both at some stage in their lives [5, 6]. After stroke around one in three individuals will sustain some degree of cognitive impairment [7] and memory deficits are commonly encountered even when physical recovery is gained [8]. Further, 10 % of individuals develop dementia soon after their first stroke and at least 30 % have dementia after recurrent stroke [3]. These cognitive deficits are not necessarily dictated by the severity of stroke and can also occur in transient or minor strokes [9].

Stroke care in the United Kingdom has been shaped by the National Service Framework for Older People

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(2001) [10] and the National Stroke strategy (2007) [11] although these do not specifically propose service organisation for patients with cognitive impairment. The Intercollegiate Stroke Working party recommends a collaborative model between primary and secondary care for long-term follow-up of those presenting with neuropsychological problems [12]. The Sentinel Stroke National Audit Programme (SSNAP) monitors whether assessment of cognition is included during routine six-month review prior to secondary care discharge, but the nature of the assessment and care pathway is not mandated. General Practitioner's (GPs) are then traditionally tasked with ongoing management of secondary prevention post-stroke to try to minimise future risk of recurrent stroke [12].

It should be noted that understanding and reducing cognitive impairment was voted the single most important topic in stroke research in a national priority setting exercise [13, 14]; thus highlighting the importance to patients. Despite this level of prioritisation and the formal organisation of stroke services, gaps in care exist for patients with cognitive and memory difficulties. The National Audit Office's report of stroke care highlighted the widespread lack of psychological services, which was also rated as the least satisfactory service in long-term care by patients [15]. Similarly, the Care Quality Commission reported that services need to address stroke-related cognitive problems [16] as only 40% of primary care trusts had good access to psychological therapy [16]. The first annual SSNAP report found that 4 in 10 people needing support for mood or memory after discharge did not get it [17]. A recent survey was carried out by the Stroke Association on 1424 stroke survivors across England detailing their own personal experiences of stroke care [18]. They found that 77% of stroke survivors have problems with memory and nearly 50% of stroke survivors reported poor support for mental fatigue and memory [18]. Although there is a focus to improve recognition of these problems by secondary care, many of these stroke-survivors may not present with cognitive deficits before discharge from specialist services. It is unclear what happens to these at-risk individuals when they are in the community. However, stroke survivors often report feeling abandoned when they leave hospital, which perhaps places emphasis on better community care and addressing psychosocial domains during rehabilitation on a par with physical recovery [18].

To improve the current model of care for stroke-survivors with cognitive and memory difficulties, it is first necessary to understand the barriers and facilitators from both the primary and secondary care perspective. This qualitative study used semi-structured interviews to describe primary and secondary care professionals' views of care received by stroke-survivors with memory/cognitive difficulties.

Methods

Sampling

An initial list of primary (General Practitioners) and secondary care clinicians (Stroke consultants and specialist nurses) in the North East of England were contacted to participate in the study. Sampling for the study was purposive and iterative to identify additional participants from the relevant specialty that might have a unique perspective. Potential participants were approached by email to take part in the study. The email included a summary of the research and gave the opportunity to ask further questions. All participants approached agreed to further contact.

Interviews

Face to face or telephone semi-structured interviews were conducted with both primary and secondary care staff (see Table 1). Interviews were conducted with 17 primary and secondary care clinicians who would be involved in the care of patients after their stroke at different stages of care. The interviews were conducted between May 2016 and February 2017 by one researcher (EYHT). The researcher (EYHT) utilised a topic guide, which evolved to ensure that emerging themes were explored. A topic guide provides a list of broad questions or areas to be covered during the interview. By

Table 1 Details of included participants

Unique Identifier	Role
NSC1	Stroke Consultant
NSC2	Stroke Specialist Nurse
NSC3	Stroke Consultant
NSC4	Stroke Consultant
NSC5	Stroke Specialist Nurse
NSC6	Stroke Physiotherapist (Rehabilitation)
NSC7	Stroke Physiotherapist (Acute Care)
NSC8	Stroke Occupational Therapist (Acute Care)
NSC9	Stroke Occupational Therapist (Rehabilitation)
PC1	General Practitioner with Specialist Interest in Dementia
PC2	General Practitioner
PC3	General Practitioner
PC4	Nurse Practitioner
PC5	General Practitioner
PC6	Practice Nurse
PC7	Nurse Practitioner
PC8	General Practitioner

responding to the data that emerged from these interviews, the topic guide evolved to address additional areas raised by participants themselves. Topics included the experience of clinicians in looking after stroke patients with memory difficulties, barriers and challenges to optimal clinical care and views on future care with emphasis on assessment for future dementia diagnoses. Participants were given the opportunity to discuss other issues they deemed important in the care of stroke-survivors with memory/cognitive difficulties. Informed written consent was obtained at the time of the interview including agreement for the interview to be audio-recorded. The interviews were transcribed verbatim. Unique identifiers were used throughout the process and any other identifiable information was removed to protect the anonymity of the participants.

Analysis

Data collection and analysis followed the principles of a thematic analysis [19]. One researcher (EYHT) familiarised himself with the data by repeated reading of the transcripts. Initial line-by-line coding was performed on the first few transcripts. A small subset of transcripts was read and subjected to coding and discussion between CE and EYHT to identify initial themes from the data. A coding framework was then developed between CE and EYHT through the application of thematic analysis [19] and codes were changed iteratively. Further analysis led to the generation of new themes and subsequent reviewing and refining of existing themes and subthemes. These themes and subthemes were subsequently grouped into broad categories to facilitate interpretation. The coding was facilitated by using a data software handling package (NVivo version 11).

Results

Barriers in current care of stroke-survivors with cognitive/memory difficulties

Less focus on memory and cognition in post-stroke care

The primary and secondary care participants repeatedly reported that post-stroke care often focussed exclusively upon the physical impact of the stroke. Although memory and cognition is not at the forefront of rehabilitation, its effects are evident as one participant remarked:

> *"With some patients you see that that doesn't actually sink in. Then you're three weeks into rehab and you've seen no change, so it can really impact on the success of the interventions that we give. Sometimes there are patients that we can't make any difference, and that's quite hard for the patient – and for therapist, as well." (NSC9, Occupational Therapist)*

Even upon discharge into the community, there is often less emphasis on communicating deficits in cognition and memory which was recognised by one primary care participant:

> *"… Memory is very rarely mentioned in the discharge letter. It's not something that is commonly mentioned, so it's not a case of, "Well, this person has had a stroke, we would recommend that this person has the MMSE [Mini-Mental State Examination] checked every six months." There is none of that; it's more to do with, "His speech is better, he's mobilising better, these are the tablets he's on, can you check his kidney function in the week?" It's that kind of thing." (PC1, GP with Specialist Interest in Dementia)*

This may well be because the focus of care for clinicians is in improving the patient's physical functioning to enable them to return home as soon as possible. This has meant that memory and cognition has not always been at the forefront of their training and practice:

> *"I think that the focus in our training, be it medical, be it nursing, be it therapy, tends to be on physical impairment, so I don't think we've got a good training base in it … Actually, it's a blind spot in many services, and not just in terms of the service as a whole, but sometimes in how we are looking at helping people who've had a stroke, I think clinicians can have a very big blind spot to cognitive problems." (NSC3, Stroke Consultant)*

However, it may well be that cognitive difficulties are not well prioritised by patients themselves and often become an after-thought rather than a main priority:

> *"At that appointment they're often worried about the speech systems or the arm weakness or the leg weakness that they had and then it's sort of, "Any other problems?" and they sort of go, "Well, the memory's not so good." It sort of comes up that way rather than it being a massive issue. So almost something that's the whole hand on the door as they're going out,'can we just tell you their memory's not as good as it was?' sort of thing." (NSC1, Stroke Consultant)*

In the community, stroke-survivors may even accept this as part of their post-stroke recovery rather than seek to rectify the issue as noticed by some professionals:

> *"A gentleman I saw recently who was … particularly in word-finding difficulty, but also some mild memory problems that he very much just lived with, and was put to one side by his family. It wasn't their primary concern, they just said, "This is how things have been since the stroke," and that was the end." (PC8, GP)*

There is a feeling for clinicians that patients themselves may underplay their symptoms but that this may be driven by their perception that there is little to be done for their symptoms:

> *"I think people might just consider it as a decline, as a general decline after the stroke, so it's something that they might have envisaged anyway, something perhaps that they think, A, isn't too serious, and B, well no-one can do anything about this anyway." (PC5, GP)*

Difficulties bringing up cognition and memory problems post-stroke

In the context of stroke, both primary and secondary care professionals recognised memory and cognition to be difficult areas to raise with patients. In secondary care this would be because of the perceived additive negative effect another potentially life-changing diagnosis could have:

> *"You've got to pick your moment, and when they come in here they get gloom and doom. The, "You're not likely to survive." The thing with a stroke as you know, it's so sudden, you get no warning for it so there's no psychological preparation for it, and it's all pretty emergency, and people aren't really taking it in. To give them another potentially devastating diagnosis I think would be quite difficult." (NSC7, Stroke Physiotherapist)*

In primary care, experience of broaching this difficult topic was similar. However, this was more about the effect it may have on patients particularly when they have recovered from their stroke physically but still had ongoing cognitive issues.

> *"Sometimes, I think, as a nurse, it's quite difficult to sit down with somebody who's doing fantastically well after their stroke, to say, "Actually, how's your memory?" It's just another whole thing. You're trying to be on a positive note saying. "You're doing really well." I think sometimes it's just difficult to actually bite the bullet and say, "How is your memory?" I think it doesn't get broached very well." (PC7, Primary Care Nurse Practitioner)*

Indeed, one participant commented that undoubtedly, some individuals would rather be seen to have a physical limitation than a cognitive one:

> *"I think they'd rather have a physical disability that can be dealt with than something that's invisible, but definitely, it's impacting on their life and the whole family's lives." (PC6, Practice Nurse)*

There may be gaps, either in structure or communication between primary and secondary care teams. Once patients have been deemed safe for discharge, according to professionals, the responsibility of care and follow-up for these deficits is then given back to the patients or at least that is what secondary care professionals expect upon discharge from the stroke service:

> *"I think, a lot of the time, we, you know, I tend to put the onus back on the patient and the relatives, say, for example. And say to them, that if they feel that it's starting to become a problem, then they should go and see their GP sooner rather than later." (NSC5, Stroke Specialist Nurse)*

However, professionals suggested that patients themselves may not wish to bring up their memory problems, mask their symptoms or even make excuses as to why things have changed so suddenly without acknowledging the potential underlying problem. This can be found in secondary care but then persist into the community:

> *"Or sometimes trying to cover up that they're having these problems, as well, wanting to appear like everything's okay." (NSC6, Stroke Physiotherapist)*

> *"I think, partly, it's a bit of, sort of, maybe some denial that," "Well, I'm getting a bit forgetful, but don't we all get like that, especially since I've been poorly?" (PC2, GP)*

Although some participants found that this may be because patients would prefer to minimise these symptoms, there were other reasons noted by clinicians. Clinicians felt that some patients had challenges communicating these symptoms:

> *"Not always, no, because I don't think they know how to verbalise it. So they would probably... It depends on the patient and the conversation you're having, but some of them might make a joke about it or it might be the spouse that brings it up and then you can sort of investigate it and question it and drill down a little bit more. But I don't think they really... I don't think they know how to say." (PC4, Nurse Practitioner)*

Lack of clarity in current services

Both primary and secondary care clinicians felt that the current service pathway was inadequate to ensure optimal management of stroke-survivors with cognitive difficulties. Time in consultation was consistently felt to be a significant barrier at all stages of post-stroke care:

"I think - It's a difficult one, because I think the way we are set up in the NHS [National Health Service], both in secondary and primary care, we don't necessarily have the time to probably care for these people how we need to." (PC2, GP)

Participants felt that this may mean that patients are not given sufficient support or indeed the relevant information regarding the sudden post-stroke changes they are facing:

"I just think that some patients and families in particular might need a bit more help to understand the impact that that aspect of the stroke has had upon the patient, and how that is impacting on their relationships, their communications, and different changes." I don't think that we necessarily spend as much time as we should on helping people understand the change, and what that means, and how that can be helped, or how that can be dealt with. It's often just taken as read, "This has happened, get on with it." (NSC3, Stroke Consultant)

A key area of concern was the lack of, or inconsistent level of, social care support for these individuals:

"Social care has got to be funded to care for these people. These people don't want to be in residential care, necessarily. They don't want to be blocking beds in hospitals. They want to be in their homes, amongst their surroundings, where it's familiar, but they need help to be able to do that. They've got to pump more money into the social care, and train up people specifically to look after these people." (PC6, Practice Nurse)

Several participants were also unsure where the care of patients should take place but recognised the limitations it would have in either setting. The current pathway of care mainly involves primary care taking over once individuals are discharged from stroke services. However, GPs reported being more reactive in the care of these patients. GPs would often watch and wait for symptoms to become more evident rather than undertaking any formal risk assessment:

"I'm not even sure how I would record that in the records, to indicate that there had been some potential impairment picked up, but no action currently required. I think I would probably be fairly reliant on that just becoming evident over time, that further assessment was required or more needed to be done. Gosh, that feels quite uncomfortable saying that, actually." (PC3, GP)

Assumptions made by healthcare professionals introducing gaps in care

It was well recognised by both primary and secondary care clinicians that there are gaps in care, particularly for stroke-survivors who go on to develop cognitive difficulties. These gaps could lead to unmet needs:

"I think there is a big number of patients who certainly have got ongoing needs that perhaps aren't having them fully addressed" (NSC8, Stroke Occupational Therapist).

Gaps in care may exist because of assumptions made by both primary and secondary care participants. Participants from primary and secondary care would often comment on what they perceived to be happening for stroke-survivors upon discharge from stroke services. Secondary care clinicians saw their roles as bringing together the information and then expect GPs to refer these individuals:

"We're [stroke clinicians] basically summarising the issues, and usually there's an expectation, unless it's very gross, that primary care will pick it up ... I think what we would probably be doing, actually, is if it's causing enough concern to the family, and the patients, we would be at that stage probably expect GPs to refer (them) into the local memory clinic service" (NSC4, Stroke Consultant)

However, according to primary care health professionals, there was an assumption that secondary care had perhaps investigated and found that no further action was required. This lack of action may well be because stroke services do not have the capacity to take on longer term cognitive issues and so redirect to the community. Primary care professionals suggested this might have the inadvertent consequence of implying to patients that GPs are disinterested because no further action is taken despite the fact that these patients still have ongoing issues:

"Well, the patient has been asked a question in a secondary care setting, and have answered that honestly, in that yes they perhaps have noticed a change in their memory. Secondary care have explored, found that there's no further action required at that time, and the patient has been discharged back to us. We've received a letter saying those things. Then we appear disinterested, potentially, and the patient's perception… That's imagining that I'm seeing it from the patient's point of view. "Well, the doctors at the hospital couldn't do anything. The GP and the doctor has taken no further action. Nobody cares. Nobody is interested. Nobody wants to do anything." Maybe how

it's interpreted, yes, now I'm thinking about it that way round. That's what makes me feel uncomfortable" (PC3, GP)

Facilitators to improve the current care of stroke-survivors with cognitive/memory difficulties

As well as barriers to care, participants were also asked about how they could improve the current care pathway. This fell into two broad categories as outlined below:

Stronger links between primary and secondary care

Links between primary and secondary care structures and staff were felt to be important to many participants. Indeed, one participant, when asked on how to ensure gaps in care were filled talked about the need for clarity in the care pathway:

"We need to be clear on when that patient actually needs to be seen again rather than leaving it as an open", "We think they're at risk, will you see them? Will you bear this in mind?" It needs to be kind of a clear pathway of saying, "Well actually this needs to be reviewed again by a certain date." (NSC2, Stroke Specialist Nurse).

To ensure this could be put in place, one participant expanded on how best to achieve this clarity. This included clear communication between the two systems:

"I think it would be useful if hospital discharge letters do mention, if there are any issues with memory, if those problems are actually mentioned on the hospital discharge letter, I think that definitely would be quite useful". Or even if the discharge letter said something like, "During assessment his MMSE score was 26 out of 30; although we're not too worried about it, I would be grateful if you could repeat it in six months." (PC1, GP with specialist interest in dementia)

Besides better communication between the two teams, participants suggested that the whole team (primary and secondary care) needed to take ownership in delivering this care:

"I don't think anybody should take sole ownership of it. I think it's up to everybody, and that's where a good MDT [multidisciplinary team] works well in a hospital. Here it works that we all do our own jobs, but we all do a little bit of everybody else's because we work very closely, so you're picking up different things. In the community, it really depends who's involved in the ongoing care. So I think everybody should have an awareness of it. It shouldn't just be one person, but then there should be some sort of pathway to follow to make sure that these patients are being given the care or the information that they need." (NSC7, Stroke Physiotherapist)

However, it was also recognised that patients should have the choice whether to access a relevant service rather than automatic enrolment onto a cognitive post-stroke pathway:

"I believe that we should have specialist stroke services available, preferably in partnership with primary care, where there is a structured follow-up available for people who want it, and where there is open access to people who don't want it, who just want to have access then." (NSC3, Stroke Consultant)

Information provision at all stages of care

The interview data suggest that information about post-stroke memory problems is not always provided in the first place or presented in a digestible format for the patient. Participants felt that it was important that the patient and their families are equipped to manage their cognitive deficits. This means that patients need to be identified as having a need and then given and taught the skills to ensure their safety in the community:

"But you need to be giving people the skills to be able to manage those risks and be able to live to whatever quality of life is possible, in a safe manner, without having to have constant health professional support. So I think it's about having that support, but also teaching skills so that people don't need that support all the time, so that you can increase their self-efficacy with dealing with their cognitive problems." (NSC6, Stroke Physiotherapist)

Participants also suggested that it is important for clinicians not to be fearful of disclosing more information, particularly if the patient and their families are keen to explore further. This may well involve charitable organisations but requires the clinician to be proactive to look out for opportunities to do so:

"Part of the role of the NHS professionals is to signpost appropriately, and maybe offer information about organisations like Alzheimer's Society. Or possibly even have a sort of direct conduit in. So there could be a formal referral at that point, if the patient and/or their carers felt that they would benefit from some support, from whoever is doing the feedback on the results. "It doesn't look as though there's another explanation for this memory impairment. In all likelihood it is a consequence of the stroke. However, there is an organisation who would be willing to offer

some support. Would you like me to ask them to make contact with you?" That would feel like an ideal way." (PC3, GP)

Finally, professionals felt that accessible information about cognitive trajectories post-stroke and when to seek help were fundamental if patients held the responsibility:

"If you notice somebody that's at risk or you notice somebody that's developed these things, you monitor and track it over time. You then have the opportunity to tell the family what kind of things to look for, what kind of things they should be prepared for, and then maybe have a chance to refer to the right people, give them the right numbers."
(NSC9, Stroke Occupational Therapist)

Discussion

This study has reported clinicians' accounts of some barriers, which they have encountered when looking after stroke-survivors with subsequent memory problems. Four key barriers were identified including: 1) Less focus on memory and cognition in post-stroke care; 2) Difficulties bringing up cognition and memory problems post-stroke; 3) Lack of clarity in current services; and, 4) Assumptions made by healthcare professionals introducing gaps in care. The relationships between these factors are also important to consider. For example, although rehabilitation of physical disabilities and a short length of stay may be the reason why there is less focus on memory post-stroke, this is compounded by the difficulties in starting conversations with patients about their cognitive difficulties. The lack of clarity in service provision means that it becomes even more difficult to ensure optimal care. Clinician participants here recognised that there is indeed a gap in the care for these individuals and have highlighted some areas which could be improved upon: 1) Stronger links between primary and secondary care; and, 2) Information provision at all stages.

It is not just clinicians who place less focus on cognitive and memory issues. In the context of stroke, the focus of rehabilitation generally is on physical recovery, as this tends to be the dominant symptom post-stroke. Indeed, one participant remarked that patients would rather have an impairment that could be seen than one such as cognition, which is not so obvious. Similarly, in a small sample of stroke patients, the patients themselves also failed to include cognitive deficits in their perception of overall recovery with the focus almost solely on the physical impairments [20]. This is despite the fact it was recognised later on that their memory loss deficits had negatively influenced their daily functional activities [20]. If clinicians struggle to discuss the issue of memory or cognitive loss and patient's themselves place less priority on these symptoms, identification will become increasingly challenging. The presence of cognitive impairment post-stroke has important functional consequences which are independent from the effects the physical impairments encountered post-stroke [21]. Emphasising the need to focus on both cognitive and physical impairments is necessary to ensure stroke survivors continue to function well in the community. This is currently a challenge, as access to psychological support is limited [22]. There are recommendations to ensure that patients' access to psychological support are as important as their access to physical support services [22] particularly for those where cognitive dysfunction only becomes apparent when they are living in the community.

Stroke patients and their caregivers require information if they are to seek help appropriately particularly with regards to cognitive and memory impairment. Patients themselves report either dissatisfaction with or a lack of information provision following a stroke [23]. Amongst health professionals this may well be because individuals are unaware which professional is providing the information [24]. Even when provided, recall of information for those with memory difficulties post-stroke poses a significant challenge for the patient and their carer [25]. Although it is assumed that stroke clinicians provide the required information post-stroke, the GP takes over this role in the community. However, evidence has shown that patients often receive the majority of their information from stroke services rather than primary care [26]. The highest risk of post-stroke dementia seems to occur in the first months post-stroke, although this may be partially due to pre-stroke cognitive impairment [27]. However a population based study with 25 year follow-up found that the cumulative incidence of post-stroke dementia was 7% at 1 year, 23% at 10 years and 48% at year 25 [28]. A further study found looked at cognition post-stroke over time. They found that although 41% were stable and 50% improved in cognition after 15 months, a significant proportion of post-stroke survivors succumbed to delayed post-stroke dementia [29, 30]. This suggests that stroke-survivors need to have adequate follow-up in the community and continual access to information and support to ensure prompt and timely diagnosis of post-stroke dementia. Stronger links between specialist and community teams could help identify those at-risk and assist in targeted cognitive assessment and follow-up.

Professionals in this study commented on the difficulties of broaching the subject of memory impairment post-stroke. When participants in this study considered the patient's perspective, they commented on patients often masking, normalising or denying the existence of

their memory loss symptoms. In the context of cognitive deficit, masking or denial of symptoms is often attributed to a barrier in the earlier diagnosis of dementia [31]. The patient's reluctance to begin conversations regarding memory concerns may well be due to an underlying fear of developing another significant life-changing diagnosis. From the clinicians' point of view, concerns about additional burden or indeed stigmatisation of patients with a diagnosis of dementia [32] and unwillingness to discuss cognitive problems with patients or caregivers [31, 33] is not unique to post-stroke care. In general a significant proportion of people with dementia remain undiagnosed [34] with groups such as those living alone, men and the oldest old may be at particular risk of missed diagnosis [35]. The additive effect of another significant symptom, particularly when stroke-survivors have recovered from their physical impairment, may contribute towards this barrier. Future work will need to explore patients' views in more detail particularly with regards to barriers in disclosing cognitive difficulties following their stroke.

The strength of this study is that we have been able to capture the views of the majority of healthcare professionals who would encounter stroke-survivors with memory or cognitive deficits post-stroke. The spectrum of views has included those in acute post-stroke care and their subsequent care in the community. There are some limitations to this study. This was a qualitative piece of research conducted in one area of England. The results may therefore not completely capture other practices nationally. However, the care pathway for stroke patients is governed by national policies to ensure a minimal standard of care and it is likely that these views are representative of other settings. In future, the experience and views resulting from alternative and international models of care may further add to our understanding of how we can improve patient care. Finally, views from patients and carers would certainly provide a vital perspective about the impact of gaps in care. We are currently undertaking data collection with these groups.

Conclusions

Cognitive and memory impairment post-stroke is common and can significantly hinder daily functioning. Health professionals involved in the care of stroke patients commented upon barriers to care, which are evident along the whole patient pathway. As recommended by experts in the field [12], there should be a focus on improvements in the coordination and cohesiveness of hospital and community care in support of stroke patients who have or are at risk of developing cognitive problems.

Abbreviations

GP: General Practitioner; MMSE: Mini-Mental State Examination; NHS: National Health Service; SSNAP: Sentinel Stroke National Audit Programme

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Availability of data and materials

The data used and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

ET conceived the framework for this study. ET collected, analysed and interpreted the data. ET prepared the manuscript for submission. BS helped to conceive the framework for this study and critically evaluated the manuscript. CP helped to conceive the framework for this study and critically evaluated the manuscript. LR helped to conceive the framework for this study and critically evaluated the manuscript. CE helped to conceive the framework for this study and assisted with the analysis of the data and contributed to the drafting of the manuscript. CE also critically evaluated the manuscript. All authors read and approve the final manuscript.

Ethics approval and consent to participate

The study was conducted in the North East of England. Ethical Approval was gained from the London – Hampstead Research Ethics Committee (reference 16/LO/0133). Before data collection began, all necessary Research and Development governance permissions were obtained. All participants provided informed written consent prior to the interview.

Consent for publication

All participants have provided informed written consented to take part in the study and for direct quotes to be used for scientific publication purposes. These have been annonymised with no identifiable personal information used.

Competing interests

The authors declare that they have no competing interests.

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5.2.1 PP3 Commentary

In this study, barriers and facilitators were identified from clinicians when describing their ability to provide ongoing care to stroke-survivors with memory deficits. In term of barriers, four themes were identified: 1) Less focus on memory and cognition in post-stroke care; 2) Difficulties in bringing up cognition and memory problems post-stroke; 3) Lack of clarity in current services; 4) Assumptions made by healthcare professionals introducing gaps in care (Tang et al., 2017a).

Deficiencies in clinical post-stroke care are not a new finding. In this study participants brought up both lack of clarity and gaps in care. Stroke is often seen and prioritised as an emergency condition which has resulted in well integrated systems to provide acute stroke care. However, the challenge has been to be establish and integrate care pathways beyond emergency and acute stroke care. (Baeza et al., 2012). There is often variability in post-hospital care and stronger links between stroke-specific clinicians, community specialists and GP are needed as highlighted by the participants in this study. This is important as the overall cost of stroke care (including informal care and lost productivity due to stroke) is around £9 billion a year (Saka et al., 2009). However, as the annual direct cost of stroke in the UK is around £4 billion, it is clear that the post-stroke care in the community is the most costly. For example, community care and informal care costs account for 32% (around £2.9 billion) and 27% (around £2.4 billion) of the overall cost respectively (Saka et al., 2009). A more recent costs analysis of stroke care has found that health care costs are expected to rise to £43 billion in 2025 and then £75 billion in 2035 with social care costs projected to rise more rapidly than unpaid care, and health care costs in the next 20 years (King et al., 2020).There is therefore a need to better understand care in the post-acute phase and to provide cost-effective interventions and care which is better suited towards individual needs. Given the frequency of cognitive deficits shortly post-stroke (Lo et al., 2019), including memory problems, earlier identification could result in earlier intervention, signposting and support which may help to reduce the costs of informal care or even costs attributed to lost productivity due to disability. Early intervention could be initiated in hospital settings and then followed-up in the community. Unfortunately, the latest annual SSNAP report has found that although there has been increase in the percentage of patients receiving mood and cognition screening before leaving hospital (from 78% (2013/14) to 93% (2018/2019), the percentage of days in hospital where patients receive psychology

input when they need it is only 10% (Sentinel Stroke National Audit Programme, 2020). This highlights the lack of inpatient psychological services for stroke patients and is not something that has improved significantly over the years given that in between 2013/14 to 2018/19, there has only been a 4% increase in the percentage of days in which psychology input is received for those that require it (Sentinel Stroke National Audit Programme, 2020). This then means that the majority of patients requiring input for their cognitive difficulties are then needed to be picked up either at their subsequent stroke reviews or when they are in the community. However, the barriers identified by the clinicians involved in their care mean that this is likely to be difficult.

The participants also highlighted some potential facilitators in the care of stroke-survivors with cognitive/memory difficulties. These included 1) stronger links between primary and secondary care; 2) information provision at all stages of care. Stronger links are needed between hospital and community settings as the patient will eventually transfer from one clinical setting to another. This transfer, however, does not equate to full cognitive recovery and so unless these links are in place, there is a risk, as evidenced by the themes identified in this study, that individuals with memory difficulties are lost to clinical services and left to manage themselves. Even up to five years after stroke, cognitive and memory difficulties are common and form part of unmet clinical and social needs (McKevitt et al., 2011). At present, given that patients are discharged from specialist services, there needs to be greater community and primary care-based strategies and involvement to plug these gaps in care. A survey of stroke-survivors confirmed that over half do want more information particularly about their stroke (McKevitt et al., 2011). A study looking at the online forum of the Stroke Association (Talkstroke) found that the main reason for forum participation was to request or offer information and support in over half or participants (De Simoni et al., 2016). In terms of forum topics, the lack of understanding of the invisible effects of stroke, which includes memory and cognitive problems, was found to be the topic generating the highest numbers of posts and users (De Simoni et al., 2016). A single six-month review is unlikely to facilitate much in the way of information provision (and retention for the recipients of this information) in the long-term. Given that information provision can have positive effects on patient and carer knowledge (Forster et al., 2012), it is likely that the transfer of information is

presented to stroke-survivors and their family throughout their stroke recovery, which does not end upon discharge from six-month stroke review.

5.3 Supporting Stroke-Survivors beyond Specialist Settings

Long-term post-stroke care recommendations, as informed by the National Stroke strategy, included the fact that all stroke survivors should have a six-month review (Department of Health, 2007a) with national clinical guidance recommending routine follow up (Intercollegiate Stroke Working Party, 2016). In general, stroke-survivors should be offered a six-month review of their stroke followed by annual reviews by the GP with the aim of picking up any persisting physical, emotional or cognitive deficits. These reviews allow patients to access clinical services for these deficits with the aim of ensuring they are supported in the community.

Previous research from a randomised control trial where the intervention was a structured re-assessment system for patients and carers at 6 months post-stroke versus existing care looked at patient independence and carer stress as outcomes but did not find any clinically significant evidence of benefit at 12 months (Forster et al., 2009). However, the long-term disabilities post-stroke i.e. beyond 12 months, have been highlighted with over a third of stroke-survivors remaining disabled 5 years post-stroke (Luengo-Fernandez et al., 2013). Although a proportion of these may end up being institutionalised, many will also be living in their own homes and therefore continue to require long term support and to be identified as needing support. In the long-term, GPs and community practitioners will therefore be managing patients and their families who are living with or assisting those with potentially significant physical, emotional and cognitive difficulties. The six-month review could therefore be used as an initial point of identification of those who are in need and then highlighted to primary care. Primary care therefore provides a central role to coordinate care from the point of specialist service discharge (Hare et al., 2006) and care beyond 6 months may be required to see clinically significant problems that need to be addressed. It may also be that regular reviews beyond a one off 6-month review in specialist settings can lead to behaviour change, ongoing review and subsequent intervention. This would then sit within the community with GPs and the primary care team. However, a survey of GPs found that only a third of respondents were aware of the need for regular reviews for stroke-survivors (Goncalves-Bradley et al., 2015). Only around half of all stroke-survivors were provided with a review and a third had no review at all. Further, even if needs were

identified 75% of GPs surveyed did not have an established protocol to address this (Goncalves-Bradley et al., 2015). The survey did find that around 80% of the reviews that were occurring, this included memory and general cognition (Goncalves-Bradley et al., 2015) suggesting that perhaps GPs themselves understood the importance of post-stroke cognitive care.

In 2018, the Stroke Association conducted their largest ever survey of stroke survivors and carers. In general nearly one in four stroke survivors felt that the follow-up care they received post-hospital discharge did not help them to cope (Stroke Association, 2018b). Specifically 1 in 5 of those surveyed felt that they needed more frequent or longer access to their GP or practice nurse (Stroke Association, 2018b). The survey found that on average people reported six different problems with their cognition with 83% of participants reporting a memory problem without much improvement in this area (Stroke Association, 2018a). Further help to deal with problems with memory was rated poorly in this survey (Stroke Association, 2018b). For patients and carers, research into cognition is amongst the top ten priorities with regards to life after stroke (Pollock et al., 2014). Therefore, it is important to identify what barriers patients with memory difficulties post-stroke and their family may face when trying to access help upon discharge from specialist services.

5.4 PP4. Post-Stroke Memory Deficits and Barriers to Seeking Help: Views of Patients and Carers.

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Qualitative Research

Post-stroke memory deficits and barriers to seeking help: views of patients and carers

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Abstract

Background. Memory and cognitive deficits post stroke are common and associated with increased risk of future dementia. Rehabilitation tends to focus on physical recovery; however, once in the community, it is unclear what happens in the longer term to the stroke-survivor with new memory difficulties.
Objective. The aim of this qualitative study was to examine in stroke-survivors what factors influence contact with health professionals.
Method. Semi-structured interviews were conducted with stroke-survivors and their family carers where memory difficulties were reported at 6 months post stroke. A topic guide was used which sought to critically examine participants care experience following their stroke diagnosis. All participants were interviewed at baseline (around 6 months post stroke) and offered an interview at around 12 months post stroke. All interviews were conducted in the North East of England. All transcripts were coded and thematically analysed.
Results. Ten stroke-survivors (age range 72–84 years) were interviewed alongside five carers at baseline; eight stroke-survivors and four carers agreed to a follow-up interview. Three main barriers were identified: (i) fear of a dementia diagnosis; (ii) denial or minimization of symptoms leading to adaptation and (iii) obstacles to seeking help in the community.
Conclusions. With an ageing population and increase in stroke-survival, the burden of post-stroke cognitive impairment and dementia will only increase. Stroke-survivors and their family carers in this study have identified issues that may hinder their presentation to health care professionals at a personal and organizational level. Health professionals need to be aware of these potential issues when planning services for stroke-survivors.

Key words: Access to care, aging, caregivers, dementia, primary care, stroke.

Introduction

Stroke is known to be a leading cause of disability worldwide with population growth and ageing being the main drivers (1). Following stroke, the individual will often not only deal with the physical impact of the stroke itself but also mental, cognitive and emotional sequelae. Post-stroke cognitive disturbances were listed in the top 10 among patients and carers in a priority-setting exercise (2). There have also been recent calls for stroke clinicians to increase attention towards the cognitive consequences often associated with stroke (3).

After a stroke, individuals report fear, lack of social confidence and loss of identity particularly in the early stages of stroke recovery (4). Although physical recovery may be evident, 'hidden' deficits such as cognitive impairment may remain unresolved with evidence showing that 90% of patients report some level of cognitive difficulty (5). In particular, post-stroke memory problems can persist in 11% to 31% of individuals 1 year post stroke (6). However, in addition to the immediate impacts of the stroke, there is also a relationship between a history of both incident and recurrent stroke with subsequent development of dementia (7). Although there may be physical recovery, post-stroke dementia will remain a significant limiting factor for survivors unless we are able to identify patients at risk of dementia earlier to ensure they get adequate access to intervention and care.

In the UK, once stroke-survivors are discharged from specialist follow-up, the task for secondary stroke prevention lies with the primary care team. The focus tends to be on the management of vascular risk factors to nationally set targets with little to no focus on the cognitive sequelae post stroke. Despite the frequency of memory and cognitive disturbance post stroke, the onus is on the stroke-survivor to approach their GP to access timely care. The aim of this study was therefore to undertake interviews in stroke-survivors with self-reported memory problems to determine what factors may affect help-seeking behaviour regarding their memory deficits.

Methods

Study design and participant sampling

Qualitative interviews were conducted with community-dwelling stroke-survivors and if applicable their family carers, who were invited to participate in the study by stroke nurse specialists during their routine 6-month post-stroke clinic review in the North East of England. Inclusion criteria were aged over 60 years and reporting subjective memory difficulties to the stroke nurse specialist. If people were interested in taking part, they were provided with a participant information sheet, and the nurse passed their details onto the study team. Upon receipt of these, purposive sampling was used and one researcher (EYHT), a medical doctor, made contact with them to provide further details and to give them an opportunity to ask questions. If participants agreed to be interviewed they were then invited to take part in interviews at baseline (following the 6-month final stroke service review), around 6-months later (around 1-year post stroke) or both.

Semi-structured interviews

Semi-structured interviews were used to elicit in detail individual's accounts and experiences when living with memory problems post stroke. A topic guide was initially formulated from review of the literature and discussion among the research team. It was designed to be iterative so that areas that were not previously identified in initial interviews could be pursued in subsequent interviews (8). These interviews were designed to seek the views of participants on a range of topics, but this paper focusses specifically on experiences of care following their stroke. The impact of their memory problems and their views on risk assessment for post-stroke dementia will be reported elsewhere. The views of clinicians have been reported elsewhere (9). Interviews were conducted in participants' home by EYHT between April 2016 and August 2017. Carers were interviewed either individually or with the stroke-survivor depending upon their preference. All interviews were audio recorded, anonymized and transcribed verbatim.

Data analysis

Data collection and analysis were an iterative process following the principles of constant comparative method (10). The data were analysed thematically (11). Data collection ceased when the researcher felt that data saturation occurred i.e. a full understanding of the participant's perspective (12) and also 'informational redundancy' had been reached (13). Initially, one researcher (EYHT) read each transcript and coded the transcripts line-by-line to identify initial themes. Two members of the team (EYHT and CE) then considered these initial themes looking for areas of overlap and categorizing them into broader themes. These were then discussed and agreed with the wider research team. NVivo 11 was used to facilitate dataset management. The paper conforms to the Standards for Reporting Qualitative Research checklist (14) (Supplementary Table 1).

Results

Ten stroke-survivors were interviewed at baseline (age range 72–84 years), five of these were conducted with carers. Eight stroke-survivors and four carers were then also interviewed 6 months later (see Table 1). One stroke-survivor declined further follow-up, and the other stroke-survivor and her family carer did not receive a

Table 1. Interview participants from stroke clinic (Interviews conducted from April 2016 to August 2017)

Unique identifier (patients and carers)	Role	Gender	Age	Ethnicity	Follow-up interview
P1	Stroke-survivor	Female	80	Caucasian	No
P2	Stroke-survivor	Female	76	Caucasian	Yes
P3	Stroke-survivor	Female	72	Caucasian	Yes
P4	Stroke-survivor	Male	75	Caucasian	Yes
P5	Stroke-survivor	Male	80	Caucasian	Yes
P6	Stroke-survivor	Male	74	Caucasian	Yes
P7	Stroke-survivor	Female	73	Caucasian	Yes
P8	Stroke-survivor	Female	82	Caucasian	Yes
P9	Stroke-survivor	Male	84	Caucasian	No
P10	Stroke-survivor	Male	79	Caucasian	Yes
C1	Carer of P1 (husband)	Male	79	Caucasian	No
C2	Carer of P4 (wife)	Female	79	Caucasian	Yes
C3	Carer of P5 (daughter)	Female	57	Caucasian	Yes
C4	Carer of P6 (wife)	Female	71	Caucasian	Yes
C5	Carer of P8 (daughter)	Female	60	Caucasian	Yes

further follow-up due to medical reasons. During interviews, participants identified and discussed barriers that prevented timely intervention and access to health services for their new memory deficits. These are presented as three main themes.

Fear of a dementia diagnosis

Interviews demonstrated that the term dementia causes fear not only as a disease but also because of the perceived subsequent ramifications associated with the disease:

> *…they can ask you questions, and they can then write down, 'Memory a bit, memory loss,' or something like that you know. I think I been frightened to tell them in case they say that, 'There's something wrong with this lady …' So I haven't, I didn't tell the doctor or anything like that about it you know I just left it because I don't want to be written down as having dementia you know. (P2)*

A perceived loss of self was found to be integral to the fear of dementia. Some participants explained how previous experiences of dementia influenced how they felt about the disease. For example, one participant spoke about her experience of her sister's dementia:

> *I hope I never turn like that … We just noticed things that she'd done all her life she couldn't cope with anymore. I looked after her as long as I possibly could, her husband had died … As I say two year ago she died, but she was in a terrible state. Really terrible, I would hate to think I ended up like that. (P7)*

Similarly, at a follow-up interview, a participant discussed the 'frightening' consequences of dementia and how it can change the individual:

> *This is what happens; you're not there, the brain's not there, you've just got the body but the brain's not there. It's such a shame to see that happening to people in the disease. I think it's worse than cancer, as far the, from the brain, anyway. The body is there but where's the, where's that person? You know, it's frightening. (P2 at 6 months)*

The term dementia also generates a sense of inevitable decline and perceived lack of useful intervention, which further exacerbates the worry surrounding the illness. Carer participants recognized that a dementia diagnosis does not necessarily equate to treatment and that support and guidance is required:

> *Well with the diagnosis not an awful lot you can do with dementia is there? Apart from monitor it. I mean if it was a diagnosis that could be, you know, stopped, the disease could be stopped, fair enough, that's a good thing. But in many ways it's going to happen, so in that case you need the more, so guidance and support of where to go next. (C5)*

The actual fear of a dementia diagnosis therefore presents an additional barrier to seeking help and access to a health care professional.

Denial or minimization of symptoms leading to adaptation

During the process of recovery from stroke, persisting issues such as memory loss can develop. However, individuals often construct rational explanations for the cause, perhaps suggestive of denial or minimizing symptoms. One carer of a stroke-survivor, who was subsequently diagnosed with dementia, reported that a diagnosis verified what they had suspected; however, the way her mother coped was through ostensible denying symptoms:

> *"My mum would be shocked, but then she'd just blank it, she would just ignore it, it hasn't happened. Because that's mum's way of doing things, of coping, that's one of her strategies she has. If she doesn't say it, or she says it enough, it'll be true." (C5)*

In this case not verbalizing a potential, second significant diagnosis seemed to help preserve her mother's mental wellbeing.

As stroke-survivors live with their memory impairment for longer, there also appeared to be a tendency to minimize or play down the significance of these symptoms:

> *It's there all the time because things come up and come up. 'Oh, I can't remember that. I've forgotten, I've just done that.' Or something, and he's like, 'Oh, it's just me, stupid me, I'm causing all this trouble.' and we're like, 'No you're not man, it doesn't matter, we can just, we'll just deal, we're used to it now.' (C3 at 6 months)*

As participants continued to live with their post-stroke memory problems, they learnt to adapt to their cognitive deficits. The data suggest that participants often increased their reliance on those around them, for example, their families, and this would lead to less urgency in help-seeking behaviour:

> *I haven't got any reason about it you know [to see anyone about memory issues … [Wife's] is always there and if, she will stop us and make us you know, stop and say you know, 'What do you want?' 'Where are you going?' … I'm not really worried about it. (P5 at 6 months)*

Furthermore, some older participants occasionally attributed their new memory deficits to 'natural' ageing. This rationale would also be shared by and with their social circles to help reassure themselves:

> *When I listen to the other women at the club, I think it's [memory problems] pretty much old age, you know what I mean? It's not anything nasty [referring to dementia]. (P3 at 6 months)*

Obstacles to seeking help in the community

Participants commented on the difficulties they had accessing care in the community through their GP; which persisted throughout their recovery. The difficulties they reported related to either their relationship with the GP or organizational aspects within primary care. In terms of GP-specific barriers, participants commented on their lack of familiarity with their GP and a lack of continuity either because of difficulty in access to their GP or because of GP working patterns:

> *He [GP] was really lovely and he would sit and talk to you. He was part of your family, but these days they're not. Our doctors as I say I have a job getting an appointment. As much as you try they will just not have it. But, when you go in they want to know exactly, you know 'Yes, what can I do for you?' and that's it … now its all part-time time, there is only one doctor full-time now in our place. (P7)*

As well as noting concerns about the continuity of relationship with GPs, participants also spoke about challenges, including the style of appointment. Many practices adopt telephone consultations alongside traditional face-to-face consultations. However, some participants commented on the positive aspects of more traditional face-to-face consultations as it was felt to be more appropriate in the context of their problems:

> *Stroke-survivor: Well, we've been talking about that I should, I should really go and ask for a consultation. Asking for an appointment for the doctor is a waste of time because you cannot-*

Carer: Well, he rings you back, doesn't he but you cannot go through all your problems on the phone. You know you're better, obviously, face to face, aren't you?
Stroke-survivor: …to sit and talk to somebody about it, like this, like we're doing here. I would like to go to the doctor's and discuss it with him because it's not easy choosing a subject and leaving it at that and saying, 'I'll come back. I'll try and get another appointment and we'll discuss B, you know we'll discuss C.' That's no, that wouldn't be any good I don't think … (P6 and C4 at 6 months)

Discussion

Summary

Memory problems following a stroke are common. It is therefore important to know what potential barriers there may be for stroke-survivors and their families to seek help for these problems. Participants in this study highlighted three areas of concern: (i) fear of a dementia diagnosis; (ii) denial or minimization of symptoms and (iii) obstacles to seeking help in the community.

Strengths and limitations

There are several strengths. We were able to capture the views of both patients and family carers, and we were able to follow-up the majority of participants. This provides a more complete picture about the care received (or not) in relation to challenges and difficulties. However, we acknowledge some limitations. The interviews were conducted by one clinician who could have influenced the answers of participants as they were aware of his professional background. Individuals were invited to participate if they reported subjective memory difficulties, which did exclude those who were unable to understand or indeed verbalize their new cognitive difficulties. This is a small sample of patients and carers from one area of England and their experience may be different to other populations. Lastly, is the issue of representativeness as all the participants were Caucasian. Indeed, barriers and challenges in accessing care may vary across different ethnic groups due to cultural perceptions of cognitive problems/dementia or language barriers when communicating difficulties to health professionals. Future studies could investigate whether barriers vary across different ethnic groups.

Comparison with existing literature

Worldwide there is a growing burden of stroke due to population growth and ageing (15). Furthermore, memory problems are commonly found after stroke alongside other cognitive impairments such as visuospatial and executive function (16). The risk of cognitive decline following a stroke is increased, and the consequences of post-stroke cognitive recovery may vary over time (17). Earlier detection of post-stroke cognitive impairment and dementia in the community could ensure patients and their families receive timely support. However, as evidenced by patient participants in this study, when living in the community, they can minimize their symptoms by adapting to their new memory deficits or perhaps even deny its existence in the first place. This can be achieved through compensation by those close to them so that they can function in the community. The fact that the support is already there as part of stroke rehabilitation may mean that individuals do not feel they need to acknowledge new symptoms such as memory loss.

Primary and secondary care clinicians have also acknowledged that there may be some difficulties in discussing memory/cognitive difficulties following a stroke (9). This may lead to further delays in diagnosing post-stroke cognitive impairment and post-stroke dementia. This in turn may delay access to appropriate interventions to ensure these individuals continue to manage well in the community. Although there is insufficient evidence to screen for cognitive impairment in the older general population (18), there have been calls to consider screening for post-stroke cognitive impairment with for example the Montreal Cognitive Assessment (19). Another approach to ensure earlier detection may be to incorporate known factors associated with cognitive decline in a risk prediction model to identify those at greatest risk of developing post-stroke cognitive impairment and dementia (17,20). However, it should be noted that denial and minimizing symptoms may well be the individual's mechanism to protect themselves from the knowledge of an impending potential diagnosis such as dementia or their focus is on the stroke itself. Screening or indeed risk assessing stroke patients for a possible dementia illness could therefore be offered but not universally applied.

Upon discharge from specialist services, primary care clinicians play an important role to ensure stroke-survivors, and their carers have access to support, information and transfered back to specialist services if symptoms arise or persist. Generally, GPs also play a fundamental role in the diagnosis of dementia (21) although at present the prevalence of undetected dementia globally remains high (22). Participants in this study were concerned about two aspects of primary care services. The first was to do with continuity of care and the second, with the method of contact i.e. telephone triage. Continuity of care is a key principle in primary care (23). It has been reported that those at the extremes of age and number of chronic conditions have placed higher value on continuity (24). There is already evidence that patients with dementia are disadvantaged by current systems (25), whereas greater GP contact may lead to recognition of a larger number of problems (26). Older stroke-survivors with memory difficulties would certainly benefit from continuity of care as their pre-existing relationship with a GP could provide an objective assessment of any new difficulties they are encountering such as memory problems. Unfortunately, the overall burden of work in primary care is increasing (27). Strategies employed by GPs to manage their workload include reducing the number of sessions i.e. part-time working (28). Participants in this study commented on this aspect of part-time working and also how they may not see the same GP twice, which will negate the advantages attributed to continuity of care. Furthermore, telephone triage has been employed extensively in primary care to manage workload, although these changes reflect a redistribution rather than reduction of workload without any cost-saving benefits (29). Participants in this study reported that telephone appointments provide an additional obstacle to accessing the appropriate care from their GP. As such, a more 'traditional' consultation approach, i.e. face-to-face, may need to be adopted to ensure that individuals with a history of stroke are able to access the care they need.

Conclusion

Although the management and knowledge around the physical sequelae post stroke is well established, cognitive issues remain a challenge. This challenge may well be hidden from health professionals as stroke-survivors and their family may not always disclose their difficulties. These include issues specific to the individual (i.e. normalization of symptoms) as well as challenges presented by current health care systems. As these individuals are likely to present in the community following specialist discharge, primary care physicians

need to be aware that there may be patients with unmet needs living in the community. This is to ensure their care needs are met when specialist services are no longer available to them.

Supplementary material

Supplementary material is available at *Family Practice* online.

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Conflicts of interest: none.

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Supplementary Table 1: Standards for Reporting Qualitative Research Checklist[1]

No.	Topic	Item	Page(s)
	Title and abstract		
S1	Title	Concise description of the nature and topic of the study Identifying the study as qualitative or indicating the approach (e.g., ethnography, grounded theory) or data collection methods (e.g., interview, focus group) is recommended	1
S2	Abstract	Summary of key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results, and conclusions	2
	Introduction		
S3	Problem formulation	Description and significance of the problem/phenomenon studied; review of relevant theory and empirical work; problem statement	3
S4	Purpose or research question	Purpose of the study and specific objectives or questions	3
	Methods		
S5	Qualitative approach and research paradigm	Qualitative approach (e.g., ethnography, grounded theory, case study, phenomenology, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g., postpositivist, constructivist/ interpretivist) is also recommended; rationale[b]	4
S6	Researcher characteristics and reflexivity	Researchers' characteristics that may influence the research, including personal attributes, qualifications/experience, relationship with participants, assumptions, and/or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results, and/or transferability	3
S7	Context	Setting/site and salient contextual factors; rationale[b]	3-4
S8	Sampling strategy	How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g., sampling saturation); rationale[b]	3-4
S9	Ethical issues pertaining to human subjects	Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	11
S10	Data collection methods	Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources/methods, and modification of procedures in response to evolving study findings; rationale[b]	3-4
S11	Data collection instruments and technologies	Description of instruments (e.g., interview guides, questionnaires) and devices (e.g., audio recorders) used for data collection; if/how the instrument(s) changed over the course of the study	4
S12	Units of study	Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	14
S13	Data processing	Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymization/deidentification of excerpts	4
S14	Data analysis	Process by which inferences, themes, etc., were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale [b]	4
S15	Techniques to enhance trustworthiness	Techniques to enhance trustworthiness and credibility of data analysis (e.g., member checking, audit trail, triangulation); rationale[b]	4
	Results/findings		
S16	Synthesis and interpretation	Main findings (e.g., interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	4-8
S17	Links to empirical data	Evidence (e.g., quotes, field notes, text excerpts, photographs) to substantiate analytic findings	4-8
	Discussion		
S18	Integration with prior work, implications, transferability, and contribution(s) to the field	Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application/ generalizability; identification of unique contribution(s) to scholarship in a discipline or field	8-10
S19	Limitations	Trustworthiness and limitations of findings	8
	Other		
S20	Conflicts of interest	Potential sources of influence or perceived influence on study conduct and conclusions; how these were managed	11
S21	Funding	Sources of funding and other support; role of funders in data collection, interpretation, and reporting	11

Reference

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5.4.1 PP4 Commentary

From a patient perspective, unmet needs post-stroke appears to be a common occurrence. A large survey with stroke-survivors had previously found that around 40% had reported memory problems, with over half reporting that this need was unmet (McKevitt et al., 2011). In this study with patients and their family caregivers, gaps in care for those who develop post-stroke cognitive problems are described. Similar to our previous paper on the views of healthcare professionals (Tang et al., 2017a), there are both personal and organisational factors which are currently acting as barriers to patients seeking further help for their post-stroke memory deficits. In this qualitative study, family caregivers and stroke-survivors were worried about a diagnosis of dementia; they also tended to deny or even minimise their symptoms and finally found obstacles with regards to the structure of primary care services (Tang et al., 2018c).

Fear of dementia is not a new concept. There have been greater efforts to raise public and professional awareness around dementia. This is because there can be some confusion particularly with regards to the early signs of dementia and normal ageing with poor knowledge of both risk and protective factors in the general public (Glynn et al., 2017). In a survey of Irish adults, substantial deficits in public knowledge of dementia were identified (Glynn et al., 2017). This lack of knowledge, particularly when it comes to the modifiable nature of the condition and the amenable risk factors associated with it may lead them to think not much can be done. It is often a lack of knowledge around the condition which may promote fear around dementia (Batsch and Mittelman, 2012). In a survey, conducted by Alzheimer 's Disease International and published in their 2012 report, they found that education/awareness was a frequent response when asked what could be done to reduce stigma (Batsch and Mittelman, 2012). In the same survey over 75% of respondents with dementia felt that there are negative associations i.e. stigma associated with dementia (Batsch and Mittelman, 2012). Charities may have an annual day or week campaign where the focus is to increase awareness. For example the Alzheimer's Society have a "Dementia Action Week (https://www.alzheimers.org.uk/get-involved/dementia-action-week)" and Alzheimer's Disease International has deemed that September is World Alzheimer's month with World Alzheimer's day on the 21st September each year (https://www.alz.co.uk/world-alzheimers-month). There has been evidence that brief exposure to information

around dementia did lead to a significant reduction in stigma (Cheng et al., 2011). Even with this heightened awareness, the focus of World Alzheimer's month (2019) was the "Let's talk about dementia: End the Stigma" campaign. It was hoped that through talking about dementia it could break down the fear and stigma surrounding dementia so that individuals could be encouraged to seek help. Contributing factors to this stigma include lack of awareness and understanding for example around the aetiology of dementia (Mukadam and Livingston, 2012) as it is particularly worse in those with limited knowledge of the disease as well as in the context of ethnicity and culture (Herrmann et al., 2018). As evidenced by the participants in this survey, stigmatic belief has been consistently identified to be a barrier to help-seeking for dementia (Werner et al., 2014, Herrmann et al., 2018). This has led to efforts to produce novel interventions to combat this stigma in general that can also be applied to stroke-survivors who are at increased risk of developing dementia. A recent example of this includes an online intervention program utilising educational and "contact" (i.e. video clips reflecting on what it is like to live and care for someone with dementia) approaches (Kim et al., 2019). Another example utilising an "intergenerational choir" compromising college students, people with Alzheimer's Disease and a family member found that not only were there benefits (i.e. reduced social isolation) for the older choir members but the college students also displayed a decrease in stigma (Harris and Caporella, 2014). Although there are interventions to reduce stigma in dementia, it should not be forgotten that worldwide, there is also stigma associated with a stroke illness (Deng et al., 2019, Sarfo et al., 2017, Hare et al., 2006). This additional stigma may further increase the reluctance for stroke-survivors to access help for their new post-stroke cognitive symptoms, further delaying earlier diagnosis of a dementia illness and access to appropriate interventions and support. Besides stigma, additional factors such as fragmented care and cognitive deficits have been found to affect recovery post-stroke (Magwood et al., 2019). As evidenced through both papers in this chapter, stroke survivors with new post-stroke memory deficits will have to overcome not only stroke-specific barriers but also the barriers associated with a potential dementia diagnosis i.e. the stigmatisation of the illness. It would be understandable therefore why perhaps a stroke-survivor, with preserved insight into their new deficits, would then wish to adapt to these deficits in order perhaps to avoid seeking further help from his or her primary care physician.

Another barrier identified by stroke-survivors and their family caregivers in this study was related to the organisational aspects of primary care. Participants talked about the importance of continuity, familiarity and also personal interaction (i.e. face to face contact) with regards to their issues. Given the perceived sensitive nature of the topic of for example a potential dementia diagnosis, it is understandable why the patient would want to discuss this with a familiar health professional. Familiarity and previous connections with the patient could also enable the healthcare professional to notice subtle differences in cognition, mood and behaviour. However, the majority of dementia diagnoses are made in secondary care by memory clinic services following referral by the GP. There is therefore an additional hurdle before a dementia diagnosis is made even if the individual is willing to attend an appointment to discuss this with his/her GP. National guidance stipulates that anti-dementia drugs should be initiated following "specialist assessment" either in clinic or in the community setting (National Institute for Health and Care Excellence, 2018). However, in recent NICE guidance, a specialist can refer to either secondary care medical specialists or other health professionals, including GP's and nurse consultants who have the "specialist expertise in diagnosing and treating Alzheimer's disease" (National Institute for Health and Care Excellence, 2018). There are currently new models of care integrating primary care services into the dementia diagnostic pathway, for example primary-care led memory clinics (Wells and Smith, 2017). One example is the Gnosall initiative which has been ongoing since 2009 (Greening et al., 2009). They have been able to utilise and mix the skills and knowledge of a consultant psychiatrist making the diagnosis, with a primary healthcare team (Greaves et al., 2015). This has resulted in patients being seen within a month from referral, minimal use of secondary care mental health services with high satisfaction with the service for all those involved i.e. patients, families and referrers (Greaves et al., 2015, Clark et al., 2013). In the South Gloucestershire primary care memory service, where GPs are asked to diagnose dementia themselves, those interviewed felt that specialist support and expertise from secondary care is still needed particularly for complex cases (Dodd et al., 2016). In general, patients themselves found both primary and secondary care led dementia pathways to be acceptable (Dodd et al., 2014). A similar primary care model could be used with emphasis placed on those who are at heightened risk such as those with recent or recurrent stroke. Some form of stratification could take place within secondary care services between those who are at high and low risk of progression

to dementia. Those at high risk could then access primary care models of care such as the examples above which would remove these apparent gaps in care. These types of primary-care led memory services may be able to overcome some of these primary-care related organisational factors particularly in the context of stroke and new cognitive deficits. It would also provide further clarity to services and where both primary and stroke healthcare professionals can reassuringly direct at-risk patients to, so that stroke patients and their family aren't left feeling unsupported.

5.5 Chapter Summary

From the accounts of patients, family caregivers and healthcare professionals, it is clear that there are a number of barriers that need to be overcome in order for potential PSD patients to be identified. There is a mixture of both personal and organisational factors that are current barriers to help-seeking behaviour by patients who develop new stroke-related cognitive deficits. There are already recognised difficulties in the general population with regards to obtaining a dementia diagnosis in the first place. These difficulties are even more prominent when you also add in a potentially disabling stroke illness. In order to overcome these barriers, we need to be able to think of innovative models or approaches to correctly identify those who wish to be identified as having a dementia illness following a stroke illness.

Chapter 6: Can we use risk prediction tools to identify post-stroke individuals at risk of dementia?

6.1 Interventions to Reduce Risk of Further Cognitive Decline Post-Stroke

In recognition of the increasing global burden of disease and overlap of at risk populations, there have been international calls for the joint prevention of stroke and dementia (Hachinski, 2015, Hachinski et al., 2018) including the Berlin Manifesto issued by the World Stroke Organisation (Hachinski et al., 2019). In theory, 90% of strokes could be prevented as ten potentially modifiable risk factors have been found to be collectively associated with around 90% of the population attributable risk for all strokes worldwide (O'Donnell et al., 2010, O'Donnell et al., 2016). Similarly, active treatment of hypertension and interventions for other risk factors such as exercise, reducing smoking, diabetes and obesity may have the potential to delay or even prevent a third of dementia cases (Livingston et al., 2017). A recent update to the evidence has found that the proportion of preventable or delayed dementia diagnoses could be as high as 40% (Livingston et al., 2020). Evidence from a population-based study that has shown concomitant reductions in stroke and dementia incidence rates over the same time period (Cerasuolo et al., 2017), suggesting that perhaps preventing stroke could also prevent some cases of dementia.

6.2. Overview of Dementia Risk Models

A number of dementia risk prediction models have been developed already (Stephan et al., 2010, Tang et al., 2015, Hou et al., 2019). A taskforce convened by the Alzheimer's Society prioritised prevention of future cases of dementia through increasing knowledge of risk and protective factors; this includes the development of life course models of dementia risk *(*Pickett *et al., 2018)*. The aim of dementia risk models is to be able to accurately predict those at the greatest risk of the disease. Earlier identification can then lead to earlier intervention and support. Challenges to this include a lack of definitive biomarkers and treatments as well as personal preferences and views as to whether the individual would want to know this information. However, there are no models currently being used clinically despite this explosion of dementia risk prediction model research and it is important to understand why this may be the case.

6.3. Dementia Risk Prediction Models in Stroke Populations

Within the context of stroke, only three models have been developed to predict post-stroke dementia (Lin et al., 2003) and cognitive impairment (Kandiah et al., 2016, Chander et al., 2017). The risk model developed to predict post-stroke dementia (n=283) at 3 months included variables such as age, occupation, number of attacks, left carotid vascular territory, right carotid vascular territory, admission NIH Stroke Scale score, admission Mini-Mental State Examination score, admission Function Independence Measure motor score (Lin et al., 2003). This model correctly classified 93.4% of patients in the development study based on these variables (Lin et al., 2003). Although neuroimaging variables do not add much to general population dementia risk models (Stephan et al., 2015), this may be different in stroke populations. A recent study looking at predictors of post-stroke cognitive impairment (PSCI) found that independent factors associated with PSCI included brain structural measures such as total grey matter volume, white matter hyperintensity volume and cerebrospinal fluid volume (Molad et al., 2019). Indeed, the two most recent risk scores for post-stroke cognitive impairment included neuroimaging variables at much shorter follow-up periods. The SIGNAL2 risk score is a seven item risk score based on variables include demographics (age and education) as well as neuroimaging variables (acute cortical infarcts, white matter hyperintensity, chronic lacunes, global cortical atrophy and intracranial large vessel stenosis) (Kandiah et al., 2016). This was similar to the CHANGE risk score which again contained demographic (age and education) as well as neuroimaging variables (chronic lacunes, hyperintensities in white matter regions, non-lacunar cortical infarct (acute) and global cortical atrophy) (Chander et al., 2017). Both models showed good discriminative accuracy (SIGNAL2 AUC=0.829, CHANGE AUC=0.74 – 0.82). However, if such as models incorporating neuroimaging variables were to be used in clinical practice, it's not clear how cost-effective or how feasible it would be to obtain such neuroimaging variables in order to facilitate these risk prediction models.

6.4. Limitations of Available Models at Present

At present, no models have been recommended for use in clinical practice for a number of reasons but an important methodological consideration is the limited amount of research in external validation of these models (Tang et al., 2015, Hou et al., 2019). Further, models will have been developed in populations with different demographics with heterogeneous cultural and medical factors, which makes

generalisability of findings challenging. External validation uses a new cohort or population independent of the development population in order to examine how reliable the model is in predicting the outcome for clinical use (Debray et al., 2015). Without this step, models may be recommended without the appropriate examination of how generalisable they are to external populations. Difficulties encountered, particularly if using for example electronic health records, include missing data, non-standardised definitions of variables required or incomplete follow-up times and event dates (Riley et al., 2016). Despite calls for this to be done previously (Tang et al., 2015), in the latest systematic review of dementia risk models, only a handful have been externally validated since (Hou et al., 2019).

There are emerging variables such as novel biomarkers (microRNAs (Shigemizu et al., 2019)) and combinations of cognitive, genetic and MRI variables (Payton et al., 2018), which have been shown to improve the accuracy of risk prediction models. In the context of stroke, the Rates, Risks and Routes to Reduce Vascular Dementia or R4VaD is an ongoing observational longitudinal study with the aim of determining the rates of cognitive impairment and dementia at least 2 years post-stroke with routine brain imaging and bloods taken for genetic analysis (http://www.isrctn.com/ISRCTN18274006). However, there has also been a lack of assessment in cost and feasibility of data gathering for the models to be used (Hou et al., 2019). Neuroimaging and genetic variables can be costly, with limited to no availability in primary care where they might be used. This is compared to more readily accessible variables such as demographic, lifestyle or health variables which tend to be recorded in electronic health records. Further, as evidenced by the fact that a GP's clinical judgement actually holds additional value in predicting dementia (Pentzek et al., 2019), it should be remembered these models only serve to guide clinicians in clinical decision making and does not replace the clinicians themselves.

Many of the models currently available have been developed in Caucasian populations (Hou et al., 2019). Racial and ethnic disparities in dementia prevalence are present (Chen and Zissimopoulos, 2018). It is felt that ethnicity may impact dementia (specifically AD) through age of onset, comorbidities, family history as well as genetic factors and cognitive change over time (Chen and Panegyres, 2016). In the context of stroke, there is some evidence that those of Black ethnicity have a higher risk of developing dementia following a stroke (Shiekh et al., 2020). On the other hand, it has also been found that incident stroke did not explain black-white

differences in cognitive decline (Levine et al., 2015b). This has led to even more models specific for example in Asian (Li et al., 2018, Park et al., 2019) populations.

Finally, given the fear and anxiety over the possibility of a future dementia diagnosis could generate, these risk prediction models need some qualitative assessment to see how appropriate and acceptable they are to use in the future. However, when presented with concepts such as dementia case finding and risk assessment, patients tend to find it difficult to grasp the key concepts (Robinson et al., 2018). The participants in this study did value earlier diagnosis but without any symptoms, the views of risk assessment for dementia varied (Robinson et al., 2018). Participants here expressed a preference for risk assessment to be embedded in routine checks for healthier lifestyles rather than specifically aimed at dementia (Robinson et al., 2018). There needs to be caution in terms of ensuring individuals understand what is involved and preferences are explored before implementing proactive approaches to be used in routine clinical practice (Robinson et al., 2018).

A first step would be to see if current dementia risk prediction models actually validate well in stroke populations.

6.5 PP5. Assessing the Predictive Validity of Simple Dementia Risk Models in Harmonised Stroke Cohorts.

Tang EYH, Price CI, Robinson L, Exley C, Desmond DW, Kohler S, Staals J, Lam BYK, Wong A, Mok V, Bordet R, Bordet A-M, Dondaine T, Lo JW, Sachdev P, Stephan BCM, STROKOG Collaboration (Stroke); 2020; 51 (7): 2095-2102

Stroke

CLINICAL AND POPULATION SCIENCES

Assessing the Predictive Validity of Simple Dementia Risk Models in Harmonized Stroke Cohorts

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BACKGROUND AND PURPOSE: Stroke is associated with an increased risk of dementia. To assist in the early identification of individuals at high risk of future dementia, numerous prediction models have been developed for use in the general population. However, it is not known whether such models also provide accurate predictions among stroke patients. Therefore, the aim of this study was to determine whether existing dementia risk prediction models that were developed for use in the general population can also be applied to individuals with a history of stroke to predict poststroke dementia with equivalent predictive validity.

METHODS: Data were harmonized from 4 stroke studies (follow-up range, ≈12–18 months poststroke) from Hong Kong, the United States, the Netherlands, and France. Regression analysis was used to test 3 risk prediction models: the Cardiovascular Risk Factors, Aging and Dementia score, the Australian National University Alzheimer Disease Risk Index, and the Brief Dementia Screening Indicator. Model performance or discrimination accuracy was assessed using the C statistic or area under the curve. Calibration was tested using the Grønnesby and Borgan and the goodness-of-fit tests.

RESULTS: The predictive accuracy of the models varied but was generally low compared with the original development cohorts, with the Australian National University Alzheimer Disease Risk Index (C-statistic, 0.66) and the Brief Dementia Screening Indicator (C-statistic, 0.61) both performing better than the Cardiovascular Risk Factors, Aging and Dementia score (area under the curve, 0.53).

CONCLUSIONS: Dementia risk prediction models developed for the general population do not perform well in individuals with stroke. Their poor performance could have been due to the need for additional or different predictors related to stroke and vascular risk factors or methodological differences across studies (eg, length of follow-up, age distribution). Future work is needed to develop simple and cost-effective risk prediction models specific to poststroke dementia.

Key Words: aging ■ dementia ■ follow-up studies ■ risk prediction ■ risk factors

Cognitive impairment is common after stroke,[1] but stroke is also a strong independent risk factor for all-cause dementia.[2] Approximately 10% of patients develop dementia soon after a first stroke, and more than a third have dementia after a recurrent stroke.[3] The incidence of dementia after stroke is ≈50× higher in the year after a major stroke compared with the general population.[4] Increasing numbers of patients are surviving a stroke, and this will lead to increasing numbers of patients later developing dementia. Reliable identification

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of those at high risk could lead to improved risk factor management, better anticipation of care needs, and an increased opportunity to benefit from interventions to reduce dementia risk,[5] including lifestyle-based interventions recently emphasized by the World Health Organization to delay or prevent cognitive decline and dementia.[6]

Poststroke dementia can be defined as any form of dementia that develops following a clinical cerebrovascular event.[7] Systematic reviews have identified over 20 different dementia risk prediction models, and they have been shown to differ in their predictive accuracy.[8–10] However, few models have been developed in a clinical setting and even fewer have been externally validated, and those that have been externally validated have had mixed results.[9,11–14] This raises the question of the applicability of such models outside the settings in which they were developed. Within the context of stroke, only 1 model has been developed to predict poststroke dementia[15] and 2 models have been developed to predict poststroke cognitive impairment.[16,17] While their predictive accuracy was found to be acceptable, the utility of such models is questionable because they all include neuroimaging variables that are costly to obtain and not easily accessible, particularly in research settings or primary care where the majority of stroke patients are followed. In addition, a previous population-based cohort study found neuroimaging variables did not significantly improve dementia risk prediction accuracy when added to a simple model incorporating sociodemographic, cognitive, health, lifestyle, functional, and genetic predictors.[18] Within the context of stroke, it is unclear whether simple prediction models excluding neuroimaging variables may be sufficient. Further, it is unknown whether dementia risk prediction models developed for the whole population will also offer accurate predictions in individuals with stroke. Thus, the aim of this study was to assess whether simple models developed to predict incident dementia in the general population also offer accurate predictions in stroke patients, which would thus permit the use of a single model to predict dementia regardless of disease subgroup.

METHODS

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Dementia Risk Models Selected for Testing

Dementia risk prediction models were selected from previous systematic reviews.[8–10] Four criteria were used to select models: (1) published predictive accuracy as measured using the C statistic or area under the curve was acceptable at ≥0.70; (2) the models incorporated variables that could be simply and easily collected in primary care and research settings (ie, models that included neuroimaging variables were not considered); (3) similar or near similar predictor variables were available in our dataset; and (4) the models included both nonmodifiable and modifiable risk factors to allow for possible future work focused on the development of risk reduction strategies. Based on these criteria, 3 models were selected: (1) the Australian National University Alzheimer Disease Risk Index (ANU-ADRI) common variables model,[14,19] (2) the Cardiovascular Risk Factors, Aging and Dementia (CAIDE) score,[20] and (3) the Brief Dementia Screening Indicator (BDSI).[21] Full details of each model are included in Table 1. Whenever possible, we used the same variables that were included in the original models. When the stroke cohorts in our study did not have the same variable, substitute variables were used. Full details of how the variables in the models were mapped in each stroke cohort and any variable substitutions that were made are provided in Table I in the Data Supplement.

Stroke Patient Sources

Individual participant data were obtained via the STROKOG (Stroke and Cognition Consortium)—an international consortium of longitudinal poststroke studies from around the world (Table II in the Data Supplement).[22] To maximize the sample size and the number of incident dementia cases to adequately test the models, we harmonized data from multiple cohorts in the STROKOG study. Four datasets were included in this analysis, but they did not all have a full set of the risk variables that we needed to test each model. Therefore, model testing is based on harmonization of different combinations of the 4 selected datasets as outlined below.

CU-STRIDE (Hong Kong)

STRIDE (Chinese University of Hong Kong–Stroke Registry Investigating Cognitive Decline) is a large cohort study (n=1007; age range, 20–98)[23] that enrolled patients consecutively admitted to an acute stroke unit of a university-affiliated hospital due to either a stroke or transient ischemic attack (TIA), excluding patients with prestroke dementia. To exclude patients with dementia before the index event, neurologists inquired about the patient's cognitive function before stroke.[23] Baseline demographic and vascular risk factors were collected, and neuropsychological assessments were performed 3 to 6 months after the index event. Participants were followed for 5 years. Psychologists administered the Clinical Dementia Rating scale, with patients suspected of having dementia being assigned a Clinical Dementia Rating of one point or more, and the diagnosis of dementia was confirmed according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, criteria.

EpiUSA (the United States)

Consecutive ischemic stroke patients ≥60 years of age (n=585) and admitted to the Columbia-Presbyterian Medical Center were recruited and followed annually for up to 10 years.[24] Initial assessments (excluding dementia diagnosis) were conducted 7 to 10 days after stroke. Neurologists specializing in stroke administered a structured neurological examination and documented any history of cerebrovascular disease and vascular risk factors. Three months and then annually after stroke, neuropsychological and functional assessments were performed, and dementia was diagnosed based on the Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised

Table 1. Description of Each Model Being Externally Validated

Model	Variables	Model Discrimination Performance	Outcome	Follow-Up Time
ANU-ADRI[14,19] (common variables model)	Age, sex, education, diabetes mellitus, smoking, and alcohol	C statistics: CVHS, 0.73 (95% CI, 0.71–0.76); MAP, 0.69 (95% CI, 0.65–0.73); KP, 0.67 (95% CI, 0.63–0.70)	Alzheimer Disease	CVHS: median, 6.0 y; MAP: mean, 3.5 (SD, 3.0) y; KP: mean, 6.0 (SD, 5.7) y
CAIDE[20]	Age, sex, education, hypertension, body mass index, cholesterol, and physical activity	Area under the curve: 0.77 (95% CI, 0.71–0.83)	Dementia	Mean, 20.9 (SD, 4.9) y
BDSI[21]	Age (65–79 y), education, stroke, diabetes mellitus, body mass index, requiring assistance with money or medications, and depressive symptoms	C statistics: CHS, 0.68 (95% CI, 0.65–0.72); FHS, 0.77 (95% CI, 0.73–0.82); HRS, 0.76 (95% CI, 0.74–0.77); SALSA, 0.78 (95% CI, 0.72–0.83)	Dementia	CHS, 6 y; FHS, 6 y; HRS, 6 y; SALSA, 6 y

ANU-ADRI indicates Australian National University Alzheimer Disease Risk Index; BDSI, Brief Dementia Screening Indicator; CAIDE, Cardiovascular Risk Factors, Aging and Dementia; CHS, Cardiovascular Health Study; CVHS, Cardiovascular Health Cognition Study; FHS, Framingham Heart Study; HRS, Health and Retirement Study; KP, Kungsholmen Project; MAP, Rush Memory and Aging Project; and SALSA, Sacramento Area Latino Study on Aging.

criteria. Following the exclusion of those who were not eligible for this study (eg, those who had dementia at baseline), 262 patients were included in the present analyses.

CASPER (the Netherlands)

The CASPER study (Cognition and Affect After Stroke: Prospective Evaluation of Risks) is a prospective cohort study (n=246; age range, 42–91) of hospital-based patients consecutively admitted with a stroke.[25] Baseline assessments were performed 10 to 12 weeks poststroke, with follow-up assessments at 6 and 12 months. Based on the Diagnostic Criteria for Vascular Cognitive Disorders: A VASCOG Statement,[26] patients with a vascular cognitive disorder (VCD) were identified, with major VCD being synonymous with dementia. It should be noted that vascular disease is considered the dominant, if not the exclusive, pathology in VCD.

STROKDEM (France)

STROKDEM (Study of Factors Influencing Post-Stroke Dementia) is a 5-year observational multicenter hospital-based prospective follow-up study of a stroke population (n=200; age range, 25–87) without dementia (https://www.clinicaltrials.gov; unique identifier: NCT01330160). Baseline and follow-up (6, 12, 36, and 60 months) evaluations included detailed cognitive and functional assessment. The Clinical Dementia Rating was used as a measure of cognitive impairment. Diagnosis of dementia was based on neurological and general clinical examinations and activities of daily living.

Incident Dementia

Dementia diagnoses, based on each study's definition of dementia, were recorded ≈12 to 18 months poststroke for each cohort. Although some studies had longer follow-up, a common follow-up time was used across the cohorts.

Inclusion Criteria

Since we wanted to assess the predictors of incident dementia after stroke, we excluded patients with TIA from the analyses. Individuals with dementia at baseline were also excluded when that information was available. We then performed our analyses in 2 rounds. The first round included all patients regardless of a history of stroke or subsequent recurrent stroke or TIA as this would be a better reflection of a stroke sample in clinical practice. In the second round, to perform a sensitivity analysis, those with a history of stroke, TIA, or intracranial hemorrhage were excluded. This would enable us to determine whether the model performance would improve in a distinct subset of stroke patients. Those who had a recurrent stroke between the baseline assessment and a follow-up assessment were also excluded from this second round of analyses when that information was available. A sensitivity analysis was done to ascertain whether there was a difference between those with a single versus recurrent episodes of stroke.

Statistical Analyses

All analyses were performed using Stata, version 15/16. Risk scores were calculated for each patient based on the 3 models and then assessed in the combined cohort as predictors of incident dementia over 12 to 18 months of follow-up. The main evaluative measures of model performance and comparison were discrimination and calibration. Discrimination refers to the ability of the model to accurately identify in 2 patients the one with and the one without the desired outcome.[27] Calibration refers to whether the observed outcomes and predictions agree.[27] We used the analytic methods that were chosen in the original publications to assess model performance. For example, logistic regression was used to assess the CAIDE score and Cox regression was used to assess the BDSI and ANU-ADRI scores. Discrimination was measured using the C statistic (Cox regression) or area under the curve (logistic regression). Calibration or model goodness of fit was tested using the χ^2 statistic for the logistic regression model and the Grønnesby and Borgan test for the Cox models. We did a complete case analysis for each risk score, that is, we only included patients if they contained all the variables of the model. Sensitivity analysis found some differences in the demographic characteristics (ie, age, sex, and educational status) between those individuals included and those individuals excluded from the analysis (Table III in the Data Supplement).

ETHICS

This study was approved by Newcastle University's Faculty of Medical Sciences Ethical Committee. The work of STROKOG has ethical approval from the University

of New South Wales' Human Research Ethics Executive. The CU-STRIDE study was approved by the Chinese University of Hong Kong–North Territories East Cluster Clinical Research Ethics Committee. EpiUSA (Epidemiologic Study of the Risk of Dementia After Stroke) was approved by the Institutional Review Board of the Columbia-Presbyterian Medical Center. The CASPER study was approved by the Medical Ethics Committee of Maastricht University Medical Center. The data provided by each study team were anonymized, and, therefore, consent was not needed.

RESULTS

Demographics for the individual and harmonized cohorts are shown in Table 2. The total harmonized sample included 1285 stroke patients with a mean age of 68.0 (SD, 10.8) years; 42.7% women. The mean follow-up was 364.3 days (SD, 52.9).

Missing Data

The proportions of missing data among the predictive variables included in each model were small to moderate (range, 0%–20.7%). See Tables IV through VI in the Data Supplement for full details of the missing data. For the BDSI model, 282 of the 406 eligible participants had complete data to evaluate the model. For the ANU-ADRI model, 1065 of the 1115 eligible participants had complete data to evaluate the model. For the CAIDE model, 873 of the 1082 eligible participants had complete data to evaluate the model.

Brief Dementia Screening Indicator

Two cohorts (EpiUSA and CASPER) were used to create the harmonized dataset for testing the BDSI model. An overview of the baseline variables is shown in Table IV in the Data Supplement. The sample included 282 patients (mean age, 65.9 years), of whom 16 developed dementia (mean follow-up, 336.0; SD, 51.7 days). The discriminative performance (C statistic) of the BDSI as mapped in the original development study and the harmonized dataset is shown in the Figure. Compared with the development cohort, the discrimination of the BDSI was low, with a wide CI (C statistic, 0.61 [95% CI, 0.42–0.79]). The model was well calibrated (χ^2=1.26; P=0.26).

ANU-ADRI (Common Variables Model)

Three cohorts (EpiUSA, CASPER, and CU-STRIDE) were used to create the harmonized dataset for testing the ANU-ADRI model. An overview of the baseline variables is shown in Table V in the Data Supplement. The sample included 1065 patients (mean age, 68.6 years), of whom 53 developed incident dementia (mean follow-up, 362.4 days; SD, 54.2). The discriminative performance of the ANU-ADRI as mapped in the original development study and the harmonized dataset is shown in the Figure. Predictive accuracy was low (C statistic, 0.66 [95% CI, 0.58–0.74]). Similar to the BDSI, the CIs were wide. The model was well calibrated (χ^2, 1.34; P=0.25).

CAIDE Score

Three cohorts (EpiUSA, CU-STRIDE, STROKDEM) were used to create the harmonized dataset for testing the CAIDE score. An overview of the baseline variables is shown in Table VI in the Data Supplement. The sample included 873 patients (mean age, 67.6 years), of whom 43 developed incident dementia (mean follow-up, 370.4 days; SD, 51.0). The discriminative performance of the CAIDE score as mapped in the original development study and the harmonized dataset is shown in the Figure. The discriminative ability of the CAIDE score was poor for predicting incident dementia (area under the curve, 0.53 [95% CI, 0.44–0.63]). The model was well calibrated (χ^2, 13.7; P=0.39).

Sensitivity Analysis

We also performed a sensitivity analysis based on patients who had had only a single stroke (Tables IV through VI in the Data Supplement; Figure). The discriminative accuracy of these models was not significantly differently compared with the total stroke cohorts, and all models were well calibrated (all P>0.05).

Table 2. Overview of Individual Stroke Cohorts and the Total Harmonized Cohort

	CU-STRIDE	CASPER	EpiUSA	STROKDEM	Total Harmonized Sample
n	650	203	262	170	1285
Age, y; mean (SD)	68.8 (11.0)	66.4 (11.6)	70.3 (7.1)	63.8 (12.5)	68.0 (10.8)
Women, %	286 (44.0)	66 (32.5)	136 (51.9)	60 (35.3)	548 (42.7)
No. of incident dementia cases, %	20 (3.1)	3 (1.5)	33 (12.6)	10 (5.9)	66 (5.1)
Follow-up time, d; mean (SD)	388.2 (31.2)	371.7 (15.5)	289.6 (53.9)	379.0 (40.1)	364.3 (52.9)

CASPER indicates Cognition and Affect After Stroke: Prospective Evaluation of Risks; CU-STRIDE, Chinese University of Hong Kong–Stroke Registry Investigating Cognitive Decline; EpiUSA, Epidemiologic Study of the Risk of Dementia After Stroke; and STROKDEM, Study of Factors Influencing Post-Stroke Dementia.

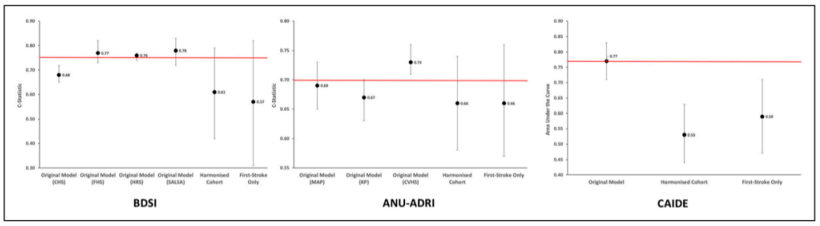

Figure. Performance of each model in the harmonized dataset.
Red line is the mean of the original development cohort area under the curve or C statistic. ANU-ADRI indicates Australian National University Alzheimer Disease Risk Index; BDSI, Brief Dementia Screening Indicator; CAIDE, Cardiovascular Risk Factors, Aging and Dementia score; CHS, Cardiovascular Health Study; CVHS, Cardiovascular Health Cognition Study; FHS, Framingham Heart Study; HRS, Health and Retirement Study; KP, Kungsholmen Project; MAP, Rush Memory and Aging Project; and SALSA, Sacramento Area Latino Study on Aging.

DISCUSSION

In this study, we used harmonized data from STROKOG to test whether 3 dementia risk prediction models developed for use in the general population would accurately predict the incidence of dementia after stroke. This would have important implications because the identification of those at the greatest risk of dementia could allow interventions to be developed to delay its onset or even reduce its incidence. We tested existing risk models in the hope that a single model could be used regardless of comorbidities such as stroke, but predictive performance at ≈12 to 18 months poststroke was low (ie, <0.70) and poorer than the performance of the original development studies.

Our study replicates previous external validation work showing poor prediction of dementia using the CAIDE score,[12,14] extending this work for the first time to individuals with stroke. This is likely to be due, in part, to methodologic differences between studies and is unsurprising considering the change in population and study duration. In the development study, the mean age of participants was 50.4 years (SD, 6.0 years) and follow-up was ≈20 years. In contrast, our study sample was older (mean age, 68.4 years) and follow-up time shorter. Previous external validation studies of the CAIDE score have also found poor transportability when it is tested in older populations[14] but not when looking at midlife risk for which it was developed.[12] Second, it is possible that other variables that are not included in the CAIDE score such as those that are related to stroke or other vascular risk factors such as diabetes mellitus may also influence dementia risk.

With regard to the BDSI model, while the age distribution was similar between our study and the original development cohort, follow-up time differed (ie, 6 years in the development study versus ≈12–18 months in our study). Previous validation studies using general population-based samples have found comparable predictive accuracy during 2 years of follow-up.[13] The BDSI includes age (1 point per year above age 65, up to 79 years of age), education (9 points), stroke (6 points), type 2 diabetes mellitus (3 points), body mass index (8 points), functional performance (ie, requiring assistance with money or medications, 10 points), and depressive symptoms or taking antidepressant medications (6 points). In the context of stroke, this points system may not accurately reflect the true impact of these risk variables, particularly with regard to diabetes mellitus, which has been shown to be associated with an increased risk of dementia[4,28] but allocated a low number of points in the BDSI model. Future work could explore both recalibration of the model in stroke-specific populations and also to test the importance of other variables that might be independently associated with dementia,[28] which could enhance predictive validity such as myocardial infarction and hypertension that are not included in this model.

The ANU-ADRI incorporates a wide range of variables, including age, sex, education, diabetes mellitus, smoking, and alcohol in the common variables model[14,19] to predict Alzheimer disease. The extended model also includes other modifiable risk factors such as physical/cognitive activity and social network/engagement.[14] The ANU-ADRI model's predictive ability was low and similar to the BDSI but better than the CAIDE score, and we found in our stroke cohort that it showed similar discriminative accuracy to one of the development cohorts, although the C statistic representing the accuracy of prediction in that development cohort was also below the acceptable range. This may be because the ANU-ADRI model is not a midlife risk model and the mean age in the original testing cohorts at baseline tended to be older.[14] However, this may also emphasize the importance of age as a risk factor, particularly given that previous studies did not find much difference between the risk prediction model and a model containing age alone.[13]

There has only been one model published for predicting poststroke dementia (Table VII in the Data Supplement).[15] It includes age, occupation, number of strokes,

left carotid vascular territory stroke location, admission NIH Stroke Scale score, admission Mini-Mental State Examination score, and admission Function Independence Measure motor score.[15] The model correctly classified 93.4% of patients 3 months after stroke.[15] We were not able to test this model due to a lack of key risk variables, including consistent magnetic resonance imaging findings, in our stroke cohort. Rather, for this study, we chose to externally validate general population-based dementia risk prediction models to determine whether a single dementia risk model could be applied. However, it is likely that acceptable predictive performance will require condition-specific data to be included. The identification of a single accurate model that had readily available variables would be of benefit to clinicians and researchers and could guide multidomain interventions.[29] Our findings do not support the use of these general population-based dementia risk prediction models, however, and instead suggest that efforts should be made to develop stroke-specific models.

Implications of Dementia Risk Prediction in Stroke

Overall, the results from our study suggest that dementia risk prediction scores developed in the general population do not work well in patients with stroke. This suggests that there are differences in risk factor profiles across disease groups. For instance, a stroke population is already at higher risk by virtue of the risk factors that led to the clinically evident cerebrovascular event. Some of these variables are already found in the dementia risk models we tested, so perhaps there is little remaining in these models to explain the additional heterogeneity in risk beyond the initial stroke event. Stroke-specific variables may be required for the development of new models in this population. They may include anatomic stroke location, type of stroke, and history of recurrent stroke, which have been found to be risk factors for poststroke dementia.[7] Although neuroimaging variables have previously been found to add little to simple risk prediction models in dementia, this was at a population level.[18] Neuroimaging variables such as white matter lesions, cerebral atrophy, and medial temporal lobe atrophy have been found to be risk factors for dementia after stroke and could be used along with stroke-specific variables in the development of stroke models.[30] However, magnetic resonance imaging is not always possible and would have significant resource implications. Harmonization of stroke cohorts is both feasible and has the potential to be used in the development of future risk prediction models, but we need to ensure that there is uniformity in how we report individual variables.

Although many of the variables in existing models may already be optimized poststroke, earlier identification of those who may have a dementia illness ensures earlier access to appropriate care and provides information that some patients, families, and clinicians value for subsequent decisions. In the context of trials, it may be that specific (eg, multidomain) interventions could be used in those at higher risk of dementia to improve or even preserve cognitive function. This has certainly been the case in those risk stratified by the CAIDE model,[29] and a similar approach could be trialed in stroke cohorts.

Strengths and Limitations

Our study has a number of strengths. We used harmonized data from 4 stroke cohorts to increase sample size and, therefore, statistical power. Furthermore, given the range of available variables, we were able to test, for the first time, 3 different dementia risk prediction models in a stroke population. However, there are some limitations. First, some variables were modified because the specific data required for the risk models were not available (Table I in the Data Supplement). This could have reduced comparability between our study and the development studies. However, we did ensure that the substitutions were as close as possible to the original definitions. Second, although the predictive accuracy of the 3 models was clearly poor, the incident dementia rate across studies was generally low, leading to wide CIs. Third, the criteria for the diagnosis of dementia varied across cohorts, in particular, one cohort (CASPER) used VCD criteria to assess dementia and not a clinical rating. This could mean that individuals could be classed as minor VCD after they were classified as major VCD at subsequent follow-ups. Our analysis was similar to previous studies' approach to the harmonization of dementia diagnoses across different cohorts (eg, see the COSMIC [Cohort Studies of Memory in an International Consortium] collaboration[31]). Fourth, the original models were generally developed in primarily white populations, which was also true in our study. We did include one South-East Asian population in the harmonized cohort for 2 of the models, although we did not specifically study the effects of ethnicity on the performance of those models. Finally, we undertook a complete case analysis, and this might have led to a select study population thereby affecting generalizability of the results. However, our sample size was large.

Conclusions

The number of individuals at risk of poststroke dementia is increasing, but there is no validated condition-specific prediction tool. The dementia risk prediction models that we studied did not perform well in our stroke cohort, underlining the importance of developing a stroke-specific model, which will likely require the inclusion of a broader range of variables that are related to stroke and vascular risk factors and careful attention to their

weightings. The next step is to use data from harmonized stroke cohorts to provide a large stroke-specific population for undertaking dementia risk prediction model development and external validation that is specific to this important subsample of individuals. We can then consider whether simple scores can be useful as the initial step in clinical monitoring of cognitive decline. The final model should permit the early identification of those individuals at the greatest risk of poststroke dementia and thus provide the opportunity for early targeted interventions.

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SUPPLEMENTAL MATERIAL

Online Supplementary Table I: Variable Substitution

Model	Original Model Variable	Score Assigned	Mapping to Harmonized Cohort
BDSI	Age	If 65 – 79 years, 1 point assigned per year above age 65	Those aged <65 were included, upper age limit was the same with those aged 79 excluded.
	Education of <12 years	9	CASPER cohort education variable was divided into low, middle and high categories. Educational level was scored in eight ordinal categories: (1) primary education, (2) lower vocational education, (3) intermediate general secondary education, (4) intermediate vocational education, (5) higher general secondary education, (6) higher vocational education, (7) higher professional education, and (8) university. Low = 1 and 2, Middle = 3 – 5, High = 6 – 8. >12 years education was equivalent to the high category.
	BMI <18.5 kg/m^2	8	As original
	Type 2 Diabetes	3	In EpiUSA, the type of diabetes was not specified. For the CASPER cohort, the type of diabetes was available but, due to a significant amount of missing data, both types of diabetes were included.
	History of Stroke	6	As original
	Needs help from others to manage money or medication	10	For the EpiUSA cohort, we used a variable representing only trouble handling money which was collected at 3 months post-stroke
	Currently takes antidepressant medications OR that "everything was an effort" ≥3 days per week over the past week	6	For EpiUSA, we relied on whether they've ever taken an antidepressant (surrogate for history of depression) and for CASPER we relied on the Hospital Anxiety and Depression score (8 or over).
CAIDE	*Age:* <47 years 47-53 years >53 years	 0 3 4	As original
	Education: ≥10 years 7 – 9 years 0 – 6 years	 0 2 3	As original
	Sex: Women Men	 0 1	As original

	Systolic Blood Pressure: ≤140 mmHg >140mmHg	 0 2	As original
	Body Mass Index: ≤30 kg/m^2 >30 kg/m^2	 0 2	As original
	Total Cholesterol: ≤6.5 mmol/L >6.5 mmol/L	 0 2	We used the STROKDEM definition of hypercholesterolemia to represent high or low levels of cholesterol.
	Physical activity: Active Inactive	 0 1	We used each study's definition of whether the individual was physically active.
ANU-ADRI	*Age for males:* <65 65 – 69 70 – 74 75 – 79 80 – 84 85 – 89 ≥90	 0 1 12 18 26 33 38	As original
	Age for females: <65 65 – 69 70 – 74 75 – 79 80 – 84 85 – 89 ≥90	 0 5 14 21 29 35 41	As original
	Educational level (years): < 8 8 – 11 >11	 0 3 6	In the CASPER dataset, we used their predefined low, middle and high categories to equate to the three categories used in the original model (see above).
	Diabetes: No Yes	 0 3	In the STRIDE cohort, this variable's coding was based on the use of a diabetes medication.
	Smoking: Never smoked Former smoker	 0 1	As original

	Current smoker	4	
	Alcohol: Abstainers Light-to-moderate Heavy	 0 -3 +3	For CASPER we used alcohol units per week in the dataset with <14 units per week used as the cut off for light/moderate group. For STRIDE, we matched their "social drinker (<1 drink per week)" category to the light-to-moderate category in the original model. The "regular drinker (1 drink or more)" category was categorized as the heavy group. For Epi USA, we coded it as the following 1) One can of beer was equated to 12 ounces of 5% alcohol equivalent to 1.8 units 2) One glass of wine was equated to 5 ounces with 12 percent alcohol content equivalent to 1.8 units 3) One liquor is equated to 1.5 oz with 40% alcohol content equivalent to 1.8 units. Again <14 units per week was used as the cut off for the light/moderate group. We only coded those who were still drinking alcohol and the alcohol unit calculations for Epi USA are based on UK guidelines.

Online Supplementary Table II: Contributions from Additional STROKOG Consortium Members

STROKOG Members
We would like to thank the following for providing data but was not used in the final analysis due to missing key variables: *Bundang VCI Cohort (Korea):* Professor Hee-Joon Bae and Professor Jae-Sung Lim *Cognitive Outcome After Stroke Cohort (Singapore):* Professor Christopher Chen and his team *Cognitive Function After Stroke Cohort (UK):* Professor Raj Kalaria ad Professor Louise Allan *Cracow Stroke Database (Poland):* Dr Aleksandra Klimkowicz-Mrowiec
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Online Supplementary Table III. Demographic characteristics of those included compared to those excluded from the external validation analysis of each model

	Included in the Analysis	Excluded from the Analysis	p-value
ANU-ADRI			
N (%)	1065 (95.5)	50 (4.5)	-
N female (%)	463 (43.5)	25 (50)	0.363
N low educational attainment (%)	572 (53.7)	23 (46.0)	0.547
Mean age (SD)	68.6 (10.3)	71.2 (11.7)	0.084
BDSI			
N	282 (69.5)	124 (30.5)	-
N female (%)	107 (37.9)	64 (51.6)	**0.010**
N low educational attainment (%)	174 (61.7)	62 (50.0)	**0.028**
Mean age (SD)	65.9 (8.6)	67.4 (6.5)	0.093
CAIDE			
N	873 (80.7)	209 (19.3)	-
% female (n)	374 (42.8)	108 (51.7)	**0.021**

% low educational attainment (n)	391 (44.8)	88 (42.1)	0.672
Mean age (SD)	67.6 (10.9)	71.4 (9.1)	**<0.001**

Key: **ANU-ADRI**, Australian National University Alzheimer's Disease Risk Index; **BDSI**, Brief Dementia Screening Index; **CAIDE**, Cardiovascular Risk Factors, Aging and Dementia score; **SD** Standard deviation

Bold text indicates where group differences were statistically significant i.e. $p<0.05$

Online Supplementary Table IV. BDSI - Harmonized Datasets for Total and First-Ever Stroke (EpiUSA and Casper)

	Total Sample			First-Ever Stroke Sample		
	Total (n=406)	**No Dementia (n=379) (n(%))**	**Incident Dementia (n=27) (n(%))**	**Total (n=288)**	**No Dementia (n=272) (n(%))**	**Incident Dementia (n=16) (n(%))**
Age (mean (SD))	66.4 (8.0)	66.0 (8.0)	71.2 (5.7)	65.9 (8.6)	65.6 (8.7)	69.9 (5.9)
Education (n(%))						
- **High Education or >=12 years**	170 (41.9)	158 (41.7)	12 (44.4)	111 (38.5)	105 (38.6)	6 (37.5)
- **Low/Middle Education or < 12 years**	236 (58.1)	221 (58.3)	15 (55.6)	177 (61.5)	167 (61.4)	10 (62.5)
BMI (n(%))						
- **≥18.5**	316 (77.8)	300 (79.2)	16 (59.3)	228 (79.2)	219 (80.5)	9 (56.3)
- **<18.5**	6 (1.5)	4 (1.1)	2 (7.4)	3 (1.0)	2 (0.7)	1 (6.3)
- **Missing variable**	84 (20.7)	75 (19.8)	9 (33.3)	57 (19.8)	51 (18.8)	6 (37.5)
Stroke (n(%))	406 (100)	379 (100)	27 (100)	288 (100)	272 (100)	16 (100)
Diabetes (n(%))						
- No	306 (75.4)	291 (76.8)	15 (55.6)	229 (79.5)	221 (81.3)	8 (50.0)
- Yes	100 (24.6)	88 (23.2)	12 (44.4)	59 (20.5)	51 (18.8)	8 (50.0)
Help Required for Money or Medications (n(%))						
- No	306 (75.4)	292 (77.0)	14 (51.9)	217 (75.4)	210 (77.2)	7 (43.8)
- Yes	85 (20.9)	73 (19.3)	12 (44.4)	59 (20.5)	51 (18.8)	8 (50.0)
- Missing variable	15 (3.7)	14 (3.7)	1 (3.7)	12 (4.2)	11 (4.0)	1 (6.3)
Depressive Symptoms (n(%))						
- No	292 (71.9)	276 (72.8)	16 (59.3)	205 (71.2)	197 (72.4)	8 (50.0)
- Yes	40 (9.9)	38 (10.0)	2 (7.4)	36 (12.5)	34 (12.5)	2 (12.5)
- Missing variable	74 (18.2)	65 (17.2)	9 (33.3)	47 (16.3)	41 (15.1)	6 (37.5)
Complete Cases (n (%))	282 (69.5)	266 (70.2)	16 (59.3)	207 (71.9)	197 (72.4)	10 (62.5)
Missing Scores (n (%))	124 (30.5)	113 (29.8)	11 (40.7)	81 (28.1)	75 (27.6)	6 (37.5)
Follow-up Time in Days (Complete Cases) (Mean (SD), Range)	336.0 (51.7), (176 – 490)	338.3 (49.7), (192 – 490)	298.7 (69.7), (176 – 434)	345.6 (46.8) (192 – 490)	347.9 (45.2) (192 – 490)	299.2 (55.8) (203 – 376)

Key: **SD,** standard deviation

Online Supplementary Table V. ANU-ADRI (Common Variables Model) – Harmonized Datasets for Total and First-Ever Stroke (Epi USA, Casper and STRIDE)

	Total Sample			First-Ever Stroke Sample		
	Total (n=1115)	**No Dementia (n=1059) (n(%))**	**Incident Dementia (n=56) (n(%))**	**Total (n=841)**	**No Dementia (n=807) (n(%))**	**Incident Dementia (n=34) (n(%))**
Age (mean (SD))	68.7 (10.4)	68.3 (10.3)	75.9 (8.9)	68.0 (10.5)	67.8 (10.5)	74.5 (9.7)
Sex (n (%))						
- Female	488 (43.8)	452 (42.7)	36 (64.3)	361 (42.9)	344 (42.6)	17 (50.0)
- Male	627 (56.2)	607 (57.3)	20 (35.7)	480 (57.1)	463 (57.4)	17 (50.0)
Education (n (%))						
- Low/Less than 8 years	595 (53.4)	561 (53.0)	34 (60.7)	453 (53.9)	432 (53.5)	21 (61.8)
- Middle/8-11 years	258 (23.1)	250 (23.6)	8 (14.3)	204 (24.3)	199 (24.7)	5 (14.7)
- High/Greater than 11 years	262 (23.5)	248 (23.4)	14 (25.0)	184 (21.9)	176 (21.8)	8 (23.5)
Alcohol						
- None	777 (69.7)	729 (68.9)	48 (85.7)	569 (67.7)	539 (66.8)	30 (88.2)
- Light-Moderate	184 (16.5)	182 (17.2)	2 (3.6)	153 (18.2)	153 (19.0)	0 (0.0)
- Heavy Drinker	105 (9.4)	102 (9.6)	3 (5.4)	80 (9.5)	77 (9.5)	3 (8.8)
- Missing variable	49 (4.4)	46 (4.3)	3 (5.4)	39 (4.6)	38 (4.7)	1 (2.9)
Diabetes (n (%))						
- No	770 (69.1)	736 (69.5)	34 (60.7)	598 (71.1)	580 (71.9)	18 (52.9)
- Yes	345 (30.9)	323 (30.5)	22 (39.3)	243 (28.9)	227 (28.1)	16 (47.1)
Smoking (n (%))						
- Never Smoked	547 (49.1)	517 (48.8)	30 (53.6)	420 (49.9)	402 (49.8)	18 (52.9)
- Former Smoker	407 (36.5)	389 (36.7)	18 (32.1)	293 (34.8)	284 (35.2)	9 (26.5)
- Current Smoker	157 (14.1)	149 (14.1)	8 (14.3)	125 (14.9)	118 (14.6)	7 (20.6)
- Missing variable	4 (0.4)	4 (0.4)	0 (0)	3 (0.4)	3 (0.4)	0 (0.0)
Complete Cases (n (%))	1065 (95.5)	1012 (95.6)	53 (94.6)	801 (95.2)	768 (95.2)	33 (97.1)
Missing Scores (n (%))	50 (4.5)	47 (4.4)	3 (5.4)	40 (4.8)	39 (4.8)	1 (2.9)
Follow-up Time in Days (Complete Cases) (Mean (SD), Range)	362.4 (54.2), (134 – 560)	363.6 (52.4), (134 – 560)	340.8 (78.4), (176 – 531)	364.9 (50.5), (134 – 541)	366.3 (48.5), (134 – 541)	333.6 (78.9), (198 – 531)

Key: SD, standard deviation

Online Supplementary Table VI. CAIDE Model – Harmonized Datasets for Total and First-Ever Stroke (Epi USA, STRIDE and STROKDEM)

	Total Sample			First-Ever Stroke Sample		
	Total (n=1082)	**No Dementia (n=1019)**	**Incident Dementia (n=63)**	**Total (n=804)**	**No Dementia (n=767)**	**Incident Dementia (n=37)**
Age (mean (SD))	68.4 (10.7)	67.9 (10.6)	75.3 (9.3)	67.7 (10.8)	67.3 (10.8)	74.6 (9.1)
Sex (n (%))						
- Female	482 (44.6)	442 (43.4)	40 (63.5)	350 (43.5)	330 (43.0)	20 (54.1)
- Male	600 (55.5)	577 (56.6)	23 (36.5)	454 (56.5)	437 (57.0)	17 (45.9)
Education (n (%))						
- ≥10 years	396 (36.6)	375 (36.8)	21 (33.3)	288 (35.8)	276 (36.0)	12 (32.4)
- 7 – 9 years	207 (19.1)	196 (19.2)	11 (17.5)	153 (19.0)	147 (19.2)	6 (16.2)
- 0 – 6 years	479 (44.3)	448 (44.0)	31 (49.2)	363 (45.2)	344 (44.9)	19 (51.4)
Hypercholesterolaemia/Total Cholesterol >6.5mmol						
- No	786 (72.6)	746 (73.2)	40 (63.5)	604 (75.1)	581 (75.7)	23 (62.2)
- Yes	187 (17.3)	175 (17.2)	12 (19.0)	132 (16.4)	124 (16.2)	8 (21.6)
- Missing variable	109 (10.1)	98 (9.6)	11 (17.5)	68 (8.5)	62 (8.1)	6 (16.2)
Systolic Blood Pressure >140mmHg						
- No	354 (32.7)	340 (33.3)	14 (22.2)	264 (32.8)	257 (33.5)	7 (18.9)
- Yes	622 (57.5)	585 (57.4)	37 (58.7)	468 (58.2)	444 (57.9)	24 (64.9)
- Missing variable	106 (9.8)	94 (9.2)	12 (19.0)	72 (9.0)	66 (8.6)	6 (16.2)
Physically Active (n (%))						
- Yes	715 (66.1)	676 (66.3)	39 (61.9)	519 (64.6)	497 (64.8)	22 (59.5)
- No	310 (28.7)	293 (28.8)	17 (27.0)	246 (30.6)	237 (30.9)	9 (24.3)
- Missing variable	57 (5.3)	50 (4.9)	7 (11.1)	39 (4.9)	33 (4.3)	6 (16.2)
BMI >30 (n (%))						
- No	795 (73.5)	758 (74.4)	37 (58.7)	602 (74.9)	580 (75.6)	22 (59.5)
- Yes	103 (9.5)	96 (9.4)	7 (11.1)	79 (9.8)	74 (9.6)	5 (13.5)
- Missing variable	184 (17.0)	165 (16.2)	19 (30.2)	123 (15.3)	113 (14.7)	10 (27.0)
Complete Cases (n (%))	873 (80.7)	830 (81.5)	43 (68.3)	666 (82.8)	640 (83.4)	26 (70.3)
Missing Scores (n (%))	209 (19.3)	189 (18.5)	20 (31.7)	138 (17.2)	127 (16.6)	11 (29.7)
Follow-up Time in Days (Complete Cases) (Mean (SD), Range)	370.4 (51.0), (176 – 645)	370.9 (49.0), (192 – 645)	359.3 (80.3), (176 – 593)	372.8 (45.4), (192 – 645)	373.5 (43.9), (192 – 645)	355.9 (73.4), (203 – 531)

Key: SD, standard deviation

Online Supplementary Table VII: Post-Stroke Models for Cognitive Impairment and Dementia

Authors (number of participants in development study)	Variables	Model Discrimination Performance	Follow-up Time	Outcome
J-H Lin et al (1) (n=283)	Age, occupation, number of strokes, left carotid vascular territory stroke location, admission NIH Stroke Scale score, admission Mini-Mental State Examination score, admission Function Independence Measure motor score	Correct classification of 93.4% of patients	3 months	Dementia
Kandiah et al (2) (n=209)	Age, education, acute cortical infarcts, white matter hyperintensity, chronic lacunes, global cortical atrophy and intracranial large vessel stenosis	AUC = 0.83 (95%CI: 0.77 – 0.88)	3-6 months	Cognitive Impairment
Chander et al (3) (n=209)	Chronic lacunes, hyperintensities in white matter regions, age, non-lacunar cortical infarct (acute), global cortical atrophy, education	AUC = 0.82 (95%CI: 0.76 – 0.88)	3-6 months	Cognitive Impairment

Key: 95%CI, 95 percent confidence interval; **AUC,** Area under the Curve

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6.5.1 PP5 Commentary

This is the first study to externally validate dementia risk prediction models in stroke populations. In order to increase the size of the population to test the models, multiple stroke cohorts were harmonised. The main aim was to assess whether risk prediction models for dementia that were developed in the general population would transport well to stroke populations. It was hoped that these models, which have been externally validated in other populations may replicate well in stroke particularly as the models chosen also used readily accessible variables that could be accessed in primary care.

Harmonisation of multiple stroke cohorts has advantages and disadvantages. The obvious advantage is that through harmonisation we are able to increase our validation cohort and therefore incident dementia cases. The benefits of increasing the size of our validation sample must then also be weighed up against limitations including missing data, availability of model variables and broad and/or differing classifications of variables across cohorts. Harmonisation of multiple cohorts was possible through the collaboration with the Stroke and Cognition Consortium (STROKOG) who have been able to also harmonise data from multiple studies and found that there was high prevalence of post-stroke cognitive impairment in diverse populations (Lo et al., 2019). A similar international consortium, the Cohort Studies of Memory in an International Consortium (COSMIC) (Sachdev et al., 2013), has previously harmonised multiple international cohorts and were able to determine the prevalence of Mild Cognitive Impairment (Sachdev et al., 2015) and determinants of cognitive performance and decline across populations (Lipnicki et al., 2019). The same methodology could possibly be used to develop dementia risk models specific for stroke populations particularly if more stroke-specific variables are to be considered.

The performance of these dementia risk models in stroke populations to predict dementia has been found to be poor. It is likely that predictors of favourable or worse cognitive outcome in the context of stroke is different. In a study looking at those with first-ever strokes or TIA without pre-existing cognitive impairment, they found that lower age and lower medial temporal lobe atrophy grade on MRI at 12 months were associated with a favourable outcome, defined as normal cognitive function or mild cognitive impairment after 7 years (Hagberg et al., 2019). Further, in a sample of stroke and TIA patients, a recent study found that 5 year risk of dementia

was associated with age, event severity, previous stroke, dysphasia, baseline cognition, low education, pre-morbid dependency, leucoaraiosis and diabetes (Pendlebury and Rothwell, 2019). Age and education continue to be persistent non-modifiable with diabetes the only vascular risk factor. Given that the models tested contained other vascular risk factors such as smoking, alcohol and high cholesterol, it is perhaps not surprising that these models do not work well in stroke populations. This may be because the stroke illness itself already takes into account the majority of these vascular risk factors and the remaining variables, except perhaps age, do not add much more predictive ability to the model. Further, a brain imaging variable in the form of leucoaraiosis, was again associated with the development of dementia and yet none of the models tested contained neuroimaging variables. It may be that modifying cardiovascular factors on its own has little affect particularly in stroke patients where the risk is already there and in theory should be well managed to prevent recurrent stroke. Certainly the Prevention of Dementia by Intensive Vascular care (preDIVA) trial looking at the effect of a multidomain cardiovascular intervention did not find a reduction in the incidence of all-cause dementia over 6 years (Moll van Charante et al., 2016). The intervention consisted of 1) assessment of cardiovascular risk factors such as smoking, diet, physical activity, weight and blood pressure with subsequent individually tailored lifestyle advice given; 2) initiation or optimisation of medication for hypertension, dyslipidaemia, type 2 diabetes and antithrombotic medication 3) educational sessions (Moll van Charante et al., 2016). This is similar to findings from the Systolic Blood Pressure Intervention Trial where intensive blood pressure control did not result in a significant reduction in the risk of probable dementia, although there were fewer than expected cases of dementia (Williamson et al., 2019). However, unlike the FINGER trial who did find that intervention in an at-risk group could improve or maintain cognitive functioning (Ngandu et al., 2015) the preDIVA study team used an unselected group of older adults and did not select those at increased cardiovascular risk (Moll van Charante et al., 2016). This may be important given that they did find that the multidomain intervention had the strongest effect among those with untreated hypertension (Moll van Charante et al., 2016).

So far, the accuracy and the validity of these models has been considered but we need to understand that for patients and their families in particular, an assessment of risk for dementia is an entirely novel approach. As assessment for a future possible dementia illness may be perceived to be different compared to an individual's cardiovascular risk. It is therefore important to understand and discuss

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dementia risk models with those at-risk of the condition such as a stroke population, so it is possible to understand the barriers and facilitators to their implementation.

6.6 PP6. The Views of Public and Clinician Stakeholders on Risk Assessment Tools for Post-Stroke Dementia: A Qualitative Study

Tang E, Price C, Stephan B, Exley C, Robinson L. (BMJ Open); 2019; 9(3):e025586

BMJ Open

The views of public and clinician stakeholders on risk assessment tools for post-stroke dementia: a qualitative study

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ABSTRACT

Objective Stroke-survivors are at increased risk of future dementia. Assessment to identify those at high risk of developing a disease using predictive scores has been utilised in different areas of medicine. A number of risk assessment scores for dementia have been developed but none has been recommended for use clinically. The aim of this qualitative study was to assess the acceptability and feasibility of using a risk assessment tool to predict post-stroke dementia.

Design Qualitative semi-structured interviews were conducted and analysed thematically. The patients and carers were offered interviews at around 6 (baseline) and 12 (follow-up) months post-stroke; clinicians were interviewed once.

Setting The study was conducted in the North-East of England with stroke patients, family carers and healthcare professionals in primary and secondary care.

Participants Thirty-nine interviews were conducted (17 clinicians and 15 stroke patients and their carers at baseline. Twelve stroke patients and their carers were interviewed at follow-up, some interviews were conducted in pairs).

Results Barriers and facilitators to risk assessment were discussed. For the patients and carers the focus for facilitators were based on the outcomes of risk assessment for example assistance with preparation, diagnosis and for reassurance. For clinicians, facilitators were focused on the process that is, familiarity in primary care, resource availability in secondary care and collaborative care. For barriers, both groups focused on the outcome including for example, the anxiety generated from a potential diagnosis of dementia. For the patients/carers a further barrier included concerns about how it may affect their recovery. For clinicians there were concerns about limited interventions and how it would be different from standard care.

Conclusions Risk assessment for dementia post-stroke presents challenges given the ramifications of a potential diagnosis of dementia. Attention needs to be given to how information is communicated and strategies developed to support the patients and carers if risk assessment is used.

Strengths and limitations of this study

- ► To the best of our knowledge this is the first qualitative study to examine critically the views of stroke patients and their family carers and clinicians about the acceptability and feasibility of a risk assessment approach to assist in earlier identification of post-stroke dementia.
- ► Understanding stakeholder views on risk assessment for dementia can help inform future strategies if risk assessment for dementia is used to assist with earlier diagnosis.
- ► The patient participants came from one area of England who were able to attend hospital outpatient departments and so may not represent the views and experiences of those with more severe post-stroke sequelae.
- ► Clinician participants came from one area of England and so may not represent the views of other service models in other regions of the UK.
- ► It is recognised that clinicians tended to be more familiar with the process of risk assessment and could elaborate further on the process involved.

INTRODUCTION

There is currently no cure for dementia and it is estimated that the worldwide economic burden will rise to US$2 trillion by 2030.[1] It has been suggested that the most powerful way to affect costs is by reducing the numbers of people who develop the illness. This may be facilitated by prediction of individual risk for the disease. Stroke is associated with an increased risk of dementia and cognitive impairment.[2–4] A recent meta-analysis found that stroke is a strong independent risk factor for dementia.[5] Stroke incidence and numbers of stroke-survivors are likely to increase due to simultaneous ageing populations and declining stroke mortality rates.[6] Given that the incidence of dementia increases exponentially with age,[1 7] this will mean that post-stroke dementia will also become increasingly prevalent. It will therefore be important to identify those at greatest risk of developing dementia following stroke in order to

implement strategies to reduce risk. In general, strategies to reduce risk of dementia may include management of cardiovascular risk factors for example, smoking, diabetes as well as regular physical activity.[8]

Risk prediction models for dementia to identify those at higher risk have been developed in whole populations[9 10] with some models specifically developed to predict cognitive impairment and dementia in stroke populations.[11–14] These stroke-specific models predict dementia or cognitive impairment over a relatively short time period (up to 18 months[14]). In spite of the expanding research in this field, none of the dementia risk prediction tools have been clinically implemented. Further, no studies have assessed the feasibility or acceptability of implementing such a strategy in a stroke population. Although risk models are currently used in everyday clinical practice in other branches of medicine, in particular prevention of cardiovascular[15] and cerebrovascular[16] disease, it is unclear how clinicians would feel about using a similar strategy to predict dementia, particularly given the stigma surrounding the diagnosis and perceived limited interventions and increased awareness of cognitive difficulties that the patients and carers may have following stroke. Further, no studies have evaluated whether using risk assessment tools for dementia would be acceptable to stroke patients themselves.

This paper presents findings from a qualitative study conducted with the patients, carers and clinicians, which, in part, sought to critically examine their views about the acceptability and feasibility of using risk prediction models in post-stroke care to identify those at greatest risk of future dementia.

METHODS

Patient and public involvement

Patients and members of the public have been involved in the development of this study from the beginning of the proposal. A participant advisory group also oversees the work conducted and annual face-to-face meetings are held to inform them of the study findings. The participant advisory group consists of members from a stroke research patient and carer panel, an organisation aimed at capturing public views about research and from a dementia and neurodegeneration specialty patient and public involvement group. The same group reviewed the study materials to ensure suitability particularly for stroke-survivors and their family carers.

Ethical approval

The study was conducted in the North East of England. Participants provided informed written consent prior to the interview.

Patient and carer sampling

Patients and carers were purposively sampled from stroke clinics that is, to ensure a mix of genders and a range carers were recruited. As part of routine clinical practice in UK stroke services, all stroke-survivors are invited to a specialist review at 6 months after the event which includes a general enquiry about memory concerns.[17] If the patient reported any subjective memory concerns at the clinic and was over the age of 60 and were able to communicate effectively in English, the stroke specialist nurse would provide further study information. Family carers were also recruited if they were involved in the stroke-survivor's care, for example, if they attended the clinic appointment with them. If potential participants were interested in taking part in the study, their details were passed onto the research team. On receipt of this information one researcher (EYHT) would make contact with the patient or carer. He would provide detailed information and an opportunity to ask questions about the study. Following their agreement to participate in the study, participants were asked to take part in an interview immediately following their 6 month review and/or around 6 months later.

Clinician sampling

General practitioners (GPs) and secondary care clinicians (eg, stroke consultants, specialist nurses, physiotherapists and occupational therapists) in the North East of England were contacted to participate in the study. Participants were given an opportunity to ask further questions. Clinicians were purposively sampled to ensure that a broad range of care professionals in both primary and secondary care were recruited.

Data collection

Interviews were conducted between April 2016 and August 2017 by one researcher (EYHT) who is a medical doctor. The topic guide was initially derived from relevant literature and expert clinical views within the research team. It was designed to be iterative to enable any topics, which had not been previously identified, to be pursued in subsequent interviews. Face-to-face semi-structured interviews were conducted with all but one participant (clinician) who had a telephone interview. The patient and family carer were interviewed individually or in pairs as requested by participants. Clinicians were interviewed individually. The part of the interviews focussing on risk assessment asked participants for their views on using risk assessment to help identify stroke-survivors who are most at risk of dementia in the future. They were also asked about the benefits and problems associated with the delivery of this assessment (eg, who and where it should be carried out), what variables could be used and how best to manage the outcome if individuals were found to be at high or low risk. At follow-up interviews, the patient and carer participants were asked to elaborate again on their views of a risk assessment process. Alongside this, the interviews also sought the views of stakeholders on the care experience of post-stroke individuals with memory problems from clinicians, patients and carers. The interviews also looked to understand the impact of post-stroke memory problems on the patients and carers. These views

on care experience from clinicians[18] and the patients and carers[19] have been reported elsewhere. The impact of post-stroke memory problems on the patients and carers will be reported separately. This paper reports the views of clinicians, patients and carers on risk assessment only. The process of risk assessment was described to participants. This was further emphasised with examples of published tools in order to highlight examples of variables used to ensure participant understanding of the process. Informed written consent was obtained from all participants prior to the interview commencing. All interviews were audio-recorded and then transcribed verbatim. To protect participant anonymity, unique identifiers were used throughout the process with identifiable personal data removed.

Data analysis

Interview data was analysed using thematic analysis[20] following the principles of the constant comparative method,[21] an iterative approach which allows for issues raised in earlier interviews to be explored subsequently. Data analysis was both deductive and inductive in that we applied learning from previous research and compared with our own data as well as inductively deriving new themes from our data. We ceased data collection when the researcher felt that data saturation occurred. This was defined as being when a full understanding of the participant's perspective[22] and also 'informational redundancy' had been reached.[23] One researcher (EYHT) familiarised himself with the dataset and subsequently coded the transcripts line-by-line. Initially, a small subset of transcripts were analysed to identify initial themes and these were discussed between CE and EYHT. Data collection and analysis was iterative and as interviews progressed, further analysis led to new themes emerging and refinement of existing themes and subthemes, which were subsequently grouped into broad categories to facilitate interpretation. The wider team (EYHT, CE, LR, BS and CP) discussed and agreed on the final categories which are presented below. For the patient and carer interviews, where follow-up interview data was also obtained, these were analysed as separate interviews to assess for any change in views over time. Data analysis continued after fieldwork had ceased. There was particular focus to understand what was important to the patients, carers and clinicians. Data analysis was facilitated by a data handing software package (NVivo V.11). The paper conforms to the standards for reporting qualitative research checklist[24] (please see online supplementary table 1).

RESULTS

In total, 30 baseline (6 month) interviews were conducted, analysed and compared including: 15 patient and carer interviews (see table 1) and 17 primary and secondary care clinician interviews (see table 2). Two pairs of participants were interviewed together at baseline. Eight stroke-survivors and four carers agreed to a further follow-up interview 6 months later with nine interviews completed. Three pairs of participants were interviewed together at follow-up. One stroke-survivor declined further follow-up and another stroke-survivor and carer were not followed up due to medical reasons. The data from this study suggest that in terms of risk assessment facilitators and barriers exist to implementation. Whereas the patient facilitators focused on the outcome of the risk assessment, clinicians focused more on the process of risk

Table 1 Interview participants (patients and carers)

Unique identifier (patients and carers)	Role	Gender	Age	Follow-up interview conducted
P1	Stroke-survivor	Female	80	No
P2	Stroke-survivor	Female	76	Yes
P3	Stroke-survivor	Female	72	Yes
P4	Stroke-survivor	Male	75	Yes
P5	Stroke-survivor	Male	80	Yes
P6	Stroke-survivor	Male	74	Yes
P7	Stroke-survivor	Female	73	Yes
P8	Stroke-survivor	Female	82	Yes
P9	Stroke-survivor	Male	84	No
P10	Stroke-survivor	Male	79	Yes
C1	Carer of P1 (husband)	Male	79	No
C2	Carer of P4 (wife)	Female	79	Yes
C3	Carer of P5 (daughter)	Female	57	Yes
C4	Carer of P6 (wife)	Female	71	Yes
C5	Carer of P8 (daughter)	Female	60	Yes

Table 2 Interview participants (clinicians)

Unique identifier (clinicians)	Role	Gender
SC1	Stroke consultant	Female
SC2	Stroke specialist nurse	Female
SC3	Stroke consultant	Female
SC4	Stroke consultant	Male
SC5	Stroke specialist nurse	Female
SC6	Stroke physiotherapist (rehabilitation)	Female
SC7	Stroke physiotherapist (acute care)	Female
SC8	Stroke occupational therapist (acute care)	Male
SC9	Stroke occupational therapist (rehabilitation)	Female
PC1	General practitioner with specialist interest in dementia	Male
PC2	General practitioner	Male
PC3	General practitioner	Female
PC4	Nurse practitioner in primary care	Female
PC5	General practitioner	Female
PC6	Practice nurse	Female
PC7	Nurse practitioner in primary care	Female
PC8	General practitioner	Female

assessment for facilitators. Both groups discussed some potential barriers associated with risk assessment focussing on the outcome.

Patient and carer views: facilitators to risk assessment focuses on the outcome of assessment

When stroke-survivors and carers discussed the concept of risk assessment, the overarching theme was that an assessment outcome was what was important, irrespective of the process and clinicians involved. Participants focused on several areas of why the outcome was important to them.

For preparation

Some stroke-survivors were generally positive about receiving a risk assessment for dementia. One stroke-survivor acknowledged that a diagnosis was something that could enable individuals to prepare themselves both at baseline and subsequently at follow-up interview:

> It's the same as knowing and not knowing, if you know that something is approaching. Not everybody is the same with the problem. You might be able to deal with it in a different way or the person supporting you, the nurse or whoever, might be able to find a different way or a more positive way of managing it. (P6, male, stroke-survivor at follow-up interview)

Similarly, for carers, there was the emphasis on what could be done following the assessment. One carer emphasised the importance of looking after the whole person, and, how earlier recognition of a potential dementia diagnosis could ensure strategies were in place to help the individual:

> But I think, if you look at the whole thing of this care of this person, if we knew earlier that you know the chances are that your memory is going to get bad and you are going to go into dementia or whatever, then we can start thinking, 'Right, well let's prop it up, let's think of ways in helping your memory as it is, to maintain the level it is before you've got no choice, it's going to get worse.' You know, maintaining what you've got and different ways of maintaining it, I think that would help. (C5, female carer (daughter) of stroke-survivor)

For timely diagnosis

For some stroke-survivors it did not matter who was performing the risk assessment for dementia or where it was undertaken. What was important was that the diagnosis was reached at the right time:

> I wouldn't say it matters, as long as it's diagnosed at the right time. (P5, male stroke-survivor)

When discussing who should perform the risk assessment, carer participants felt that primary care and the community were regarded as being optimal because of the existing GP-patient relationship. This is because the GP has an overall view of the individual's care:

> I think if you've got a good relationship with your GP I think it should be that, it should be them. Yeah, because you know you trust them you build up a relationship with them so I think that probably, for me that would be the one. (C4, female carer of stroke-survivor)

For reassurance

When stroke-survivor participants were asked about a structured risk assessment process, a further participant reported that the outcome could also ensure some reassurance, either that their symptoms were not related to a dementia diagnosis or that a diagnosis of dementia would be accompanied by support:

> I think it's reassurance a lot of reassurance with people. You have to give them that to tell them, that 'We are there with you. We're going to be helping you.' And that's you know, I think that's a good thing. (P2, female stroke-survivor)

Patient and carer views: barriers to risk assessment focuses on the outcome of assessment

Anxiety around a potential diagnosis of dementia

Some carers commented on how the outcome from risk assessment could generate worry and anxiety because of the potential diagnosis of dementia:

> To be honest, I don't know if it would help somebody saying, 'You're like this, you're upset because you're like this now, but we actually think you're going to get much worse.' Do you know what I mean? (C3, female carer (daughter) of stroke-survivor)

This person's opinion did not change when she was followed up 6 months later. The participant's focus was again on worrying about what could develop and how not knowing about one's risk would actually be more preferable:

> If you could find out and then say, 'Right, we've got this medication, or something, that can help you,' maybe. But if they're just going to tell you, and then you've got this hanging over your head, and you're thinking, 'When is it going to start?' and then you'd be thinking you'd forget something and you'd think, 'Oh, that's it, it's coming', which it would be quite normal if you hadn't had that diagnosis, you'd think, 'Well I just forgot something, everybody does that. (C3, female carer (daughter) of stroke-survivor at follow-up interview)

However, one carer felt that despite the worry a potential diagnosis may generate, the benefit of this would be to find strategies to maintain cognitive function:

> I think if you had earlier diagnosis, then you would be sort of prepared before things got difficult to handle, or before problems arise, that would be a very good thing. The disadvantages as you say, alarming the

carers or the patients themselves, 'I'm going to lose my mind.' Because, particularly in the older generation, that's a big worry to them. It is a big worry, it's a big worry to all of us, but to older people particularly. (C5, female carer (daughter) of stroke-survivor)

Concerns about how it may affect their recovery

Not all stroke-survivors were as keen to engage in risk assessment, as there was emphasis on how this may affect them psychologically particularly when their physical deficits had recovered enough to allow them to return to a more usual routine. Therefore, although diagnosis was felt to be important, whether an individual would like to know was also dependent on their subsequent post-stroke recovery:

> That's difficult you know because I mean if you have an early diagnosis you know and say, well 'It's going to happen' you know but at the moment now I seem to be progressing through, I'm driving now, you know I'm going back to meetings and whatever. I wonder whether an early diagnosis would restrict that. (P4, male stroke-survivor)

This was particularly evident when the patients were followed up 6 months later. One participant had actually changed her view over time. Although she had initially felt positive about the process, she then changed her mind when questioned on the same process at her follow-up interview:

> I think my thinking has gone the other way for knowing about that. I think it's sad. I think it's a sad thing. I really do, I think it's really sad that for people to know that they're going to be at high risk, it's a sad thing for it to happen to people, and I don't think I'd want to be one of the sad people. I think I'd just want to be, potter along and that's it. (P2, female, stroke-survivor at follow-up interview)

At follow-up interviews participants also felt that risk assessment should be an individual choice because of the ramifications of the assessment outcome that is, a potential diagnosis of dementia. Although clinicians may deem it to be helpful, the choice to undergo risk assessment needs to be a weighed up, which should negate any calls for it to be made a universally applied process:

> I think, medically speaking, yes. On the other hand, does it give people things to worry about that they wouldn't have worried about if you hadn't done the tests? So, I think it depends really on your personal point of view. Do you want to be, you see I would look on the test as saying, well you're at a low, you've got a low risk so that's great but then if it turned out you'd got a high risk are you going to be more worried and less happy than you were before. It's hard to really balance it, isn't it? (P3, female, stroke-survivor at follow-up interview)

Clinician views: facilitators to risk assessment focusses on the process

Clinicians discussed facilitators to risk assessment in terms of how the process may affect the individual and also how the process could be implemented in the future.

When discussing how to implement this process, both primary and secondary care specialists discussed the advantages associated with hosting this process within their own individual teams.

Process familiarity in primary care

For primary care, it was about the fact that risk assessment was already a familiar process but that it needed to be individualised:

> I think it's a good tool. We're quite good at using tools, aren't we, but there's always going to be exceptions to the rules and you've got to individualise what you do with it … But sometimes using a score or a tool is a way into a service. (PC4, nurse practitioner in primary care)

It was also recognised by one GP that although there is familiarity with risk assessment in primary care, there needs to be caution that the system is not overwhelmed with such tools:

> I do quite like risk profiling. I think we went a little bit crazy with the risk profiling. And there feels to be a lot of competing risk profiling tools, that we're getting a little bit inundated with at the moment … So I think anything like this, I love, if it can be incorporated and brought on to an individual and needs level - so you can think about caring, identifying risk and needs for an individual - would feel great for me. (PC2, general practitioner)

Secondary care provides specialist input

Stroke care clinicians discussed the facilitators of risk assessment within a specialist setting. This was based on the fact that they felt a responsibility to ensure that post-stroke sequelae are followed up in their specialist services due to the multidisciplinary element of their standard practice and easier access to services. This was particularly important to ensure information could also be given to the patients at a time when they may need it the most:

> I think the 6 month review tends to be a period of time when the patient's acute side, acute phase of their care has kind of been established, and this is probably the time when they start to recognise problems. And I think it should be within a stroke MDT (multidisciplinary team), not so much focused on by GP's, as such. (SC2, stroke specialist nurse)
>
> Well, you need the right support. You need people that actually understand stroke. So I think it would have to be delivered by stroke healthcare professionals. And I think you get so much information when you're initially an inpatient, I think maybe

that's not the best place to do it … Yeah, it's a big thing to be told that you might develop dementia in a few years' time, so you need psychologists kind of available for if someone needs counselling as a result of that finding. I think it's tricky. (SC6, stroke physiotherapist)

Collaborative care

Primary care clinicians commented that there may be a place for both primary and secondary care to work together in identifying those at risk.

I think primary care would be a completely reasonable place to do that. I guess it's a conversation that could start at diagnosis, at discharge from hospital, like actually, we know that people who have had a stroke are at higher risk of having dementia, these are the things to be aware of, and you know to start that discussion (PC8, general practitioner)

Primary and secondary care clinicians felt that such a shared care pathway needed to be formalised to reduce the risk of individuals falling into gaps in care:

… even if it was picked up in secondary care it's still going to be primary care where most of the management is occurring. So I think it being identified at the 6 month follow-up, but then there being a formal sort of mechanism, in which primary care pick it up and process it, would be fine. (PC3, general practitioner)

I don't mind where work is done, provided that it is done in a structured and standardised way. If that be, if that can be in primary care that is really good, because that is the long-term follow-up, long-term support, integrating the community … just as long as it can be delivered in a systematic way, and people don't fall through gaps or get inconsistent care. (SC3, stroke consultant)

Further, the process of communication between primary and secondary care could also be used in the diagnostic process. It was felt that repeated assessments could help facilitate diagnosis by identifying trends in symptoms:

You can measure a trend, can't you, if you're using something and measuring something, you can look at a trend. So if its, depends on the type of tool, I guess. But if you did it at you know at the 6 months review date and then we did it subsequently a year later in primary care, you would see any changes or decline or improvement. So it's a way of, it's a way of monitoring a trend on how they're doing, I guess. So I don't, I don't see any reason why it couldn't be done in both and used across both. I don't think we use enough across both. (PC4, nurse practitioner in primary care)

Clinician views: barriers to risk assessment focusses on the outcome

Limited interventions available

Similar to the perspectives of carers, clinicians recognised the anxiety that a risk assessment process might generate and felt that it should be a personal choice to undertake an assessment because of the perceived lack of intervention:

Yeah, I think I would, I would have degree of anxiety, especially given that the measures that we're putting in place are … that we could put in place are largely supportive rather than preventative … I would be less confident that I could be giving my patient advice to say, Well, if we do this, and we do this, and if we do this and you do that then that might move you into an even smaller risk group. (PC3, general practitioner)

Outside research trials, I'm not convinced that there is a definitive value in doing that yet. You know if we get really overwhelming evidence that it's amenable to intervention so you know there's all the theory about blood pressure, and statins, and all the rest of that, but my reading of the evidence on all of that at the moment is that the jury is out whether it makes a difference to cognitive function. So yeah, I'm not convinced that identifying risk, unless you've got a something you can do about it, is actually sensible. (SC4, stroke consultant)

Anxiety around a potential diagnosis of dementia

In recognising the anxiety that this process may generate, one clinician also commented on the fact that the patients may not be willing to engage in conversation over the subject of dementia and care should be taken when discussing a potential diagnosis of dementia.

I think it's good if we tell them that we're looking through and saying, 'Look, you know there could be a problem here.' But for every single patient, again, because it's quite a still a – not a taboo subject – but it's still not something that people want to talk about … I don't know whether it would be used on every single 'per', you know what I mean, like, everybody. (SC5, stroke specialist nurse)

No change from standard practice

The majority of clinical participants wanted to know, not only what the outcome of the risk assessment would be, but also the resulting care the patient would receive. As part of current routine clinical care, all stroke-survivors are offered annual reviews in order to ensure their vascular risk factors for example, blood pressure and cholesterol are well controlled. In terms of reducing risk, one primary care physician expressed concerns as to what the benefit would be to the individual if risk factor modification was already in place anyway, particularly with regards to the emotive side of a potential dementia diagnosis. A secondary care specialist questioned the value when there was seemingly limited interventions that

could be implemented besides managing their cardiovascular risk:

> I guess you've got to be very clear about what it is that you're going to be doing differently for them. So I can see the value if you use a tool for kind of primary prevention, then you're kind of selecting a group of patients out to do something particular with, but I just wonder what would be different about what you do with a risk assessment tool for people who have already had a stroke, when really you know already that it is all about managing their cardiovascular risk so I'm not sure that you would be doing anything different for them. (PC8, general practitioner)

> Many people will not know of the association between dementia and stroke and many people would not want to know if they were at risk of dementia and again, if you're identifying somebody at risk of a condition that you can't do anything about, what's the right stage to, to do that? However, many of the things you need to do in terms of people being at risk of dementia are the same of the general cardiovascular. So, I'm not sure that there is anything additional that needs to be done about reducing people's risk for dementia over and above general cardiovascular risk. (SC3, stroke consultant)

DISCUSSION

Main findings

This is the first study to explore key stakeholders' - stroke-survivors, family carers and primary and secondary care clinicians - views on the use of a risk assessment process to predict future dementia in stroke-survivors. It is clear that some of the participants interviewed believed that risk assessment could be of clinical use, but raised concerns about it being mandatory. Clinicians highlighted both the benefits of collaborative and individual (ie, primary or secondary) care if dementia risk assessment for stroke-survivors was to be implemented.

Clinician facilitators suggest benefits in either primary or secondary care settings, but also in a collaborative model of care between the two. This latter finding echoes recommendations from the UK Intercollegiate Stroke Working Party for a collaborative care model, linking community and specialist care, with the aim of integrated long-term follow-up for those presenting neuropsychological problems.[17] Although both primary and secondary care clinicians could see the benefits of carrying this assessment in their own specialties, some of the patients and carers in this study valued their relationship with their GP. Further, primary care clinicians themselves are familiar with the process of risk assessment. A survey of primary care physician trainees found that they were also keen to implement a dementia risk assessment strategy to assist in earlier identification.[25] However, potential barriers have been identified in previous studies, such as system-related factors (lack of support, time constraints)[26 27] and training in dementia,[27] which would need to be addressed. Risk assessment is an objective process requiring specific individual variables for example, age, gender and education. Such data is readily available in primary care in many countries where electronic medical record systems are in place. Further, GPs are already asked to assess cardiovascular risk as part of routine clinical care.[28] However, some GPs themselves do not like using risk assessment tools particularly as the tools do not provide the support needed in communication.[29] Training in communicating the risk assessment process, particularly in the context of dementia, would be required if this were to be implemented in clinical practice. Further, some models, particularly those developed in stroke populations[11] may also include variables such as complex imaging data, which will only be available in secondary care and may be difficult to obtain even in specialist settings. If risk assessment were to be conducted in primary care, then the risk assessment models utilising data which can be accessed in primary care, needs to be externally validated in stroke populations to assess their accuracy.

Clinician participants were concerned about whether risk assessment would actually change standard practice. In a stroke population, it is unclear whether identifying those at risk would achieve any additional benefit from a risk factor modification point of view. This is because stroke-survivors already receive annual community follow-up with particular focus on vascular risk factor modification. However, current evidence suggests that development of post-stroke dementia is more than just about vascular risk and would require a different approach for example, psychological support, cognitive preservation strategies and additional resources. Results from several trials, assessing whether vascular-based interventions can reduce dementia risk, have been largely disappointing.[30 31] These results suggest that perhaps an individual's risk of post-stroke cognitive impairment and dementia includes risk factors beyond vascular risk. Inflammation following a stroke seems to have both positive and negative effects and whether lowering inflammation can prevent post-stroke dementia will need to be addressed in future trials.[32]

Currently population screening for dementia is not recommended due to a lack of evidence evaluating risks and benefits,[33] despite positive views from older adults.[34] Risk assessment can target high-risk groups rather than the general population. Recent evidence has found a decline in age-specific incidence of dementia, particularly in high-income countries, suggesting that rising levels of education and modifying cardiovascular risk may have driven a decline in dementia risk.[35 36] Indeed, the importance of modifiable risk factor reduction for dementia was reported in the World Alzheimer Report (2014)[37] and around a third of Alzheimer's disease cases worldwide might be attributable to modifiable risk factors.[38] Risk assessment tools use these modifiable risk factors to predict risk. Similar to other branches of medicine where risk assessment is used to predict risk of a future illness,

it would be hoped that this approach could reduce one's risk of future dementia. Stroke affects more than 100 000 people in the UK per year,[39] creating a large population with cognitive deficits and/or at high risk of future decline who may benefit from risk assessment for dementia. However, participant groups in this study, particularly clinicians, reported that given the potential ramifications of risk assessment, individuals should be given the choice of whether to undergo assessment. Some stroke-survivors were positive about such an approach, but agreed that it should be up to the individual and the family rather than applied universally. Participants in this study recognised the anxiety this process could generate particularly when the perceived possible interventions for dementia are limited. The National Institute for Health and Care Excellence have recently updated their guidance and have concluded that case finding should only be conducted as part of a clinical trial, which also provides an intervention.[40] Therefore, careful discussion needs to be adopted with the the patient and their carers before undertaking such a process in any setting. In the context of the dementia diagnostic journey, transition from living with an undiagnosed memory problem to being diagnosed with a dementia illness is underpinned by uncertainty.[41] Although risk assessment certainly does not provide any certainty for a dementia illness, the discussions and objective evaluation using the tools may help the individuals process their current condition and assist in the preparation for a potential diagnosis of dementia. Preparation was mentioned by participants in this study as a facilitator for risk assessment.

Clinical implications

Case finding for dementia involves actively assessing individuals at risk of a future dementia illness, which at present is only recommended in clinical trial settings due to a lack of post-assessment intervention.[42] Once a suitable intervention is found however, the views of those conducting the assessment and the recipients of such an assessment will need to be assessed. Similarly there will be challenges with regards to assessment of capacity when performing risk assessment for this at-risk population. It is also important to note that GPs find communicating the diagnosis of dementia difficult.[43] Although risk assessment is not providing a diagnosis of dementia, careful consideration will be required in training health professionals in communicating the concept of risk for a disease such as dementia. From this study we have identified the priorities according to each stakeholder group which would need to be addressed prior to clinical implementation in the future.

Limitations

The participants in this study came from one area of England and were Caucasian. The patient participants were also well enough to attend outpatient assessment clinics. Future studies could look to explore views in other populations including views from minority ethnic groups, the patients with more severe stroke-related impairments and different service models. Due to familiarity, it is recognised that clinicians expanded more around the risk assessment process. Despite this being the case, the patients and carers were given the opportunity to understand the concept of risk assessment as part of the interview process, but the emphasis on a need for a diagnosis and good care was what was important for them. Participants were also aware that the interviewer was also a primary care clinician, which may have the potential to introduce bias into participant responses. This is because a clinician interviewer may be viewed as an expert and judge in clinical decision making and moral judgements made.[44] On the other hand interviews tend to be broader in scope and richer in data when conducted by a clinician researcher.[44] Further, both clinical and non-clinical members contributed to the analysis of the data to minimise the effect this may have had.

CONCLUSIONS AND FUTURE RESEARCH

Timely recognition of those at risk of dementia is crucial to enable individuals early access treatment and support. Although dementia screening after stroke is not yet advocated on preventative grounds, assessing risk has some potential benefits for individuals who make an informed choice to participate. There would need to be better cohesiveness of communication between primary and secondary care, with more support placed in the community. Further, it should be recognised that if risk assessment were to be incorporated into clinical practice, this will potentially place additional burdens on a dementia diagnostic service, which is already overstretched. Next steps are to identify which tool to use, how best to manage those who are deemed high-risk individuals and whether there are any interventions, which can reduce their risk. Future studies will need to look specifically at what factors put a stroke-survivor at risk that could be potentially modified and also whether there are specific interventions suitable to a post-stroke population to reduce risk.

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Contributors ET conceived the framework for this study. ET collected, analysed and interpreted the data. ET prepared the manuscript for submission. CE helped to conceive the framework for this study and assisted with the analysis of the data and contributed to the drafting of the manuscript. CE also critically reviewed and edited the manuscript. CP helped to conceive the framework for this study, assisted with the analysis of the data and critically reviewed and edited the manuscript. BS helped to conceive the framework for this study, assisted with the analysis of the data and critically reviewed and edited the manuscript. LR helped to conceive the framework for this study, assisted with the analysis of the data and critically reviewed and edited the manuscript.

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Ethics approval Ethical Approval was obtained from the London – Hampstead Research Ethics Committee (reference 16/LO/0133).

Provenance and peer review Not commissioned; externally peer reviewed.

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Supplementary Table 1

Standards for Reporting Qualitative Research Checklist[1]

No.	Topic	Item	Page(s)
	Title and abstract		
S1	Title	Concise description of the nature and topic of the study identifying the study as qualitative or indicating the approach (e.g., ethnography, grounded theory) or data collection methods (e.g., interview, focus group) is recommended	1
S2	Abstract	Summary of key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results, and conclusions	1
	Introduction		
S3	Problem formulation	Description and significance of the problem/phenomenon studied; review of relevant theory and empirical work; problem statement	1 - 2
S4	Purpose or research question	Purpose of the study and specific objectives or questions	2
	Methods		
S5	Qualitative approach and research paradigm	Qualitative approach (e.g., ethnography, grounded theory, case study, phenomenology, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g., postpositivist, constructivist/ interpretivist) is also recommended; rationale[b]	2
S6	Researcher characteristics and reflexivity	Researchers' characteristics that may influence the research, including personal attributes, qualifications/experience, relationship with participants, assumptions, and/or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results, and/or transferability	2
S7	Context	Setting/site and salient contextual factors; rationale[b]	2
S8	Sampling strategy	How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g., sampling saturation); rationale[b]	2
S9	Ethical issues pertaining to human subjects	Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	2 and 9
S10	Data collection methods	Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources/methods, and modification of procedures in response to evolving study findings; rationale[b]	2
S11	Data collection instruments and technologies	Description of instruments (e.g., interview guides, questionnaires) and devices (e.g., audio recorders) used for data collection; if/how the instrument(s) changed over the course of the study	2 - 3
S12	Units of study	Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	3
S13	Data processing	Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymization/deidentification of excerpts	3
S14	Data analysis	Process by which inferences, themes, etc., were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale [b]	3
S15	Techniques to enhance trustworthiness	Techniques to enhance trustworthiness and credibility of data analysis (e.g., member checking, audit trail, triangulation); rationale[b]	3
	Results/findings		
S16	Synthesis and interpretation	Main findings (e.g., interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	3 - 7
S17	Links to empirical data	Evidence (e.g., quotes, field notes, text excerpts, photographs) to substantiate analytic findings	3 - 7
	Discussion		
S18	Integration with prior work, implications, transferability, and contribution(s) to the field	Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application/ generalizability; identification of unique contribution(s) to scholarship in a discipline or field	7 - 8
S19	Limitations	Trustworthiness and limitations of findings	8
	Other		
S20	Conflicts of interest	Potential sources of influence or perceived influence on study conduct and conclusions; how these were managed	8
S21	Funding	Sources of funding and other support; role of funders in data collection, interpretation, and reporting	8

Reference

1. O'Brien BC, Harris IB, Beckman TJ, et al. Standards for reporting qualitative research: a synthesis of recommendations. *Academic medicine : journal of the Association of American Medical Colleges* 2014;89(9):1245-51. doi: 10.1097/acm.0000000000000388 [published Online First: 2014/07/01]

6.6.1 PP6. Commentary

This paper brings together the views of stroke-survivors, their family care givers and clinicians from the interviews that were conducted. In this study, barriers and facilitators were identified to risk assessment for stroke patients. All three groups agreed that one barrier was the perceived anxiety generated from a potential diagnosis of dementia. Patients and carers were also worried about how it may affect their recovery and clinicians were concerned about the limited interventions that were available even if risk assessment could identify those who need further help (Tang et al., 2019). The facilitators discussed included reassurance of what these symptoms may mean, enabling patients and carers to be prepared and for a diagnosis to be obtained. Primary care clinicians talked about how there was familiarity around risk assessment whereas secondary care clinicians discussed the need for specialist input. However, there was a recognition on the value of collaborative primary care and secondary care pathways (Tang et al., 2019).

Chapter 5 highlighted the fears and stigma surrounding a dementia diagnosis. In this chapter, patients and their caregivers also discussed how a potential diagnosis may then affect them particularly if they have started to resume normal daily activities. This highlights some additional challenges around screening and case finding that was discussed in Chapter 2. It has been previously discussed in Chapter 5 about the importance of collaborative and better interface between primary care to look after these individuals. Here when discussing risk assessment, there was a similar feeling about perhaps using the expertise across the primary and secondary care spectrum particularly with regards to a risk assessment process. When considering the use of risk assessment tools, there certainly needs to be a balance between the accessibility of risk model variables and also model accuracy. Variables which are difficult to obtain because it may only be found in specialised settings such as MRI may also be more costly to obtain. However, if they do indeed improve dementia risk models then perhaps, they do need to be incorporated in some way. One approach suggested by Licher et al, has been a stepwise approach with a basic model (age, history of stroke, subjective memory decline and need for assistance with finance or medication; C-statistic 0.78) being used in primary care and an extended model incorporating cognitive testing, brain MRI parameters and genetic data (C-statistic 0.86) being used in specialised settings (Licher et al., 2018a). These complimentary models are able to predict dementia with some degree of certainty at 10 years follow-up, which would allow time for intervention prior to the onset of the

dementia syndrome (Johnson and Asthana, 2019). Interestingly in the basic model for the study by Licher et al, three of the four variables can be found in the Brief Dementia Screening Indicator (Barnes et al., 2014), which did not perform well in our external validation study in stroke patients. Further, as the incidence of dementia is nearly 50 times higher in the year after a major stroke, it may well be that in order to incorporate variables such as MRI predictors, we need to consider developing a stroke-specific dementia risk prediction model for use in secondary care settings rather than primary care as a) these specialised settings should have these variables to hand b) it minimises the delay between onset of memory or cognitive complaints and then access to memory services.

6.7 Chapter Summary

Although there is emerging evidence in the useful application of these risk models in the context of trials, there are some limitations in their potential clinical use. Certainly, at present these tools should not be offered universally, however there will be people who may appreciate an earlier diagnosis or perhaps even an explanation of their perceived change in cognition. Further, stroke-specific models need to be developed if their use clinically were to be considered. The question remains as to where they may potentially sit in clinical services.

Chapter 7: Gaining Consensus to Improve the Care of Stroke-Survivors with Cognitive Deficits

7.1 Current Clinical Services

The National Service Framework for Older People (2001) (Department of Health, 2001) and the National Stroke strategy (2007) (Department of Health, 2007b) both contain recommendations that all stroke-survivors and their carers should receive regular reviews of their health and social care needs. Structured health and social care review at 6 months, 12 months and then annually after a stroke is also recommended in the National Clinical Guidelines for Stroke (Intercollegiate Stroke Working Party, 2016). The review at six months following discharge from hospital is to ensure that stroke-survivors are supported in the community and that ongoing access is provided to services as needed. This includes a consideration for further specialists assessment if there are psychological changes (Intercollegiate Stroke Working Party, 2016). The Sentinel Stroke National Audit Programme (SSNAP) provides a national register of stroke care in England, Wales and Northern Ireland aiming to measure both the quality and organisation of stroke services (Sentinel Stroke National Audit Porgramme). As part of SSNAP, memory and cognition assessment are considered by recording whether patients were screened for mood, behaviour or cognition since discharge in clinical records. (https://www.strokeaudit.org/SupportFiles/Documents/Clinical-Datasets-and-Help-Notes/SSNAP-Core-Dataset-4-0-0.aspx). The Greater Manchester Stroke Assessment Tool (GM-SAT) has been described as a feasible and acceptable post-stroke assessment tool that provides a structured and systematic way to approach the six-month review (Rothwell et al., 2013, Bamford et al., 2013). The GM-SAT has also been used by the Stroke Association when they conduct their post-stroke reviews (https://www.stroke.org.uk/professionals/life-after-stroke-services/post-stroke-review). The GM-SAT includes a specific question about whether the stroke-survivor has had any difficulty with memory, concentration and attention. It has been updated to GMSAT2 in order to include those living in care homes so that it can support reviews for all stroke-survivors (https://clahrcprojects.co.uk/news/gm-sat-re-launch).

A previous audit of six-month reviews found that despite these recommendations and a structured assessment tool, only a quarter of clinical commissioning groups were offering six month reviews with some services not being

able to provide this service to all stroke-survivors in their locality (Walker et al., 2014). One possible reason for this poor provision may be due to a lack of clear policy guidance in terms of service requirements (Walker et al., 2014). With regards to post-stroke care, annual reviews of post-acute organisational SNNAP audit are able to provide an overview of where further improvements could be made to improve stroke clinical care. The most recent SSNAP audit annual report found that only around 32% of patients are receiving a six-month assessment (Sentinel Stroke National Audit Programme, 2020). At present, between 2013 to 2019, the proportion of those receiving a six month review has only increased from 20% to 32% (Sentinel Stroke National Audit Programme, 2020). To address this, the National Stroke Programme aims to ensure three times as many patients receive 6-month reviews of their recovery and needs (Stroke Association, 2019). Despite the perceived benefits of such reviews, there are no apparent benefits at 12 months following a structured reassessment system for patient and their carers at 6 months post-stroke (Forster et al., 2009). This may be because the intensity of the intervention may not have been sufficient to affect problems 6 months after stroke-onset (Forster et al., 2009). It should be noted that cognition is only a small proportion of this review with many other areas needing to be addressed, and it cannot be assumed that more in depth cognitive assessment would not be beneficial. As evidenced by the findings from the qualitative study in chapter 5, there is often less focus on cognition during holistic assessment, so perhaps there needs to be more specific attention or guidance given to clinicians conducting the six-month review.

7.2 Service User Experiences

A previous study has reported that patients and carers have found the six-month review to be a useful mechanism to discuss their concerns but were uncertain about its purpose (Abrahamson and Wilson, 2019a). It's becoming clear, that a standardised structured assessment has its limits particularly when there is a lack of focus with regards to a patient's concerns. There have been recommendations that the six month review be patient-led and for a more "targeted" approach (Abrahamson and Wilson, 2019b). Cognitive difficulties are a common unmet need (Chen et al., 2019a) with as many as 9 out of 10 stroke survivors reporting impact on at least one cognitive function where 83% described problems with their memory (Stroke Association, 2018b). In chapter 6, the role of a clinically useful risk assessment model was discussed. A risk assessment approach could gauge individualised risk,

but one consideration may then need to be about what to do with the result. It was therefore important to bring together the findings of the previous work presented in this thesis to stroke clinicians to explore how we could improve the care and identification of those at the greatest of risk of further cognitive decline post-stroke.

7.3 PP7. Care Priorities for Stroke Patients Developing Cognitive Difficulties: A Delphi Survey of UK Professional Views.

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Care priorities for stroke patients developing cognitive difficulties: a Delphi survey of UK professional views

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Abstract

Background: Post stroke cognitive difficulties are common but generally prioritised below other impairments. In the UK, clinical guidelines recommend a holistic review at six-months post-stroke including an assessment of cognitive function. In order to assist clinicians to provide better care for patients with post-stroke cognitive deficits and assist with service planning, our aim was to establish professional consensus on key actions at the six-month review.

Methods: An electronic Delphi survey was developed with ten potential actions for clinicians to prioritise across five different clinical scenarios describing patients with cognitive difficulties. Scenarios varied in terms of age of the stroke-survivor, stroke severity and use of dementia risk assessment. A panel of professional volunteers was obtained through the British Association of Stroke Physicians and the UK National Stroke Nursing Forum.

Results: Forty-five stroke clinicians completed round one, with 21 participants completing round two. Priorities consistently supported by professionals included access to psychological services, screening for a mood disorder and ensuring multi-professional input. Direct access to specialist memory services was not generally supported unless a dementia risk assessment tool indicated that the individual was at high risk of dementia.

Conclusions: Assessment of post-stroke cognitive deficits needs to be routinely considered during the six-month review. A formal risk assessment tool could be a way to streamline direct access to memory clinic services to ensure that individuals at-risk of dementia receive ongoing care.

Keywords: Stroke, Cognition, Risk assessment, Dementia, Delphi

Background

Stroke is a leading global cause of mortality, disability and high economic burden due to the costs of treatment and subsequent care [1]. In the United Kingdom (UK), the national healthcare strategy has identified stroke as a clinical priority and aims to improve rehabilitation for stroke-survivors upon discharge [2]. Although the focus here is often on physical recovery, in the first-year post-stroke 4 in 10 patients display some degree of cognitive impairment without a diagnosis of dementia [3]. This can be linked to demographic and illness factors. Around 6 months post-stroke, females with a history of cerebrovascular disease and those who had either a lacunar or posterior circulation infarct are more likely to have developed a new cognitive impairment [4]. The identification of dementia is also more challenging due to additional persistent deficits post-stroke, both with global cognition and individual domains e.g. attention and processing speed, memory, language and frontal

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executive function can be affected [5]. A history of stroke is also a strong independent risk factor for dementia [6]. It accelerates the onset of dementia by 10 years [7] and 10% of individuals develop dementia soon after their first stroke [8].

National Clinical Guidelines recommend clinical neuropsychology or clinical psychology provision for severe or persistent disturbance in cognitive function after stroke, with routine follow-up [9]. As part of long-term post-stroke care, the National Stroke strategy had previously recommended that all stroke survivors should have a six-month review [10] although the clinician conducting these reviews can vary [11]. This was further emphasised in care guidelines produced by the National Institute for Health and Care Excellence [12]. The latest national audit of clinical services via the Sentinel Stroke National Audit Programme, reports that these reviews are conducted by a stroke coordinator (32.8%), therapist (10%), secondary care clinician (10.5%), district/community nurse (10%), a General Practitioner (0.1%), voluntary services employee (9.9%) or others (26.7%) [13]. At the six-month review, clinicians are encouraged to enquire about any cognition problems. However, a national audit of post-acute services found that there are still a number of areas where 6-month reviews are not being performed [14]. Further, a survey was conducted by a UK charity, the Stroke Association of 1424 stroke survivors from across England who detailed their own personal experiences of stroke care which was carried out between January to March 2016. They found that 77% of stroke survivors have problems with their memory with nearly 50% rating the support they received for memory problems and fatigue as poor [15].

In order to assist clinicians and service planners in providing targeted care for stroke-survivors with subsequent new cognitive issues, we sought professional views about areas of high and low priority during the six-month review. We chose this time point as it would be more likely to reflect long-term and stable post-stroke sequelae as opposed to a shorter time where deficits could be due to the immediate impact of a stroke illness. As current assessment guidance remains generic, we attempted to ascertain whether care priorities should reflect differing patient characteristics.

Methods

Delphi participants

Two professional societies, the British Association of Stroke Physicians (BASP) and the National Stroke Nursing Forum (NSNF) agreed to disseminate the Delphi survey to their members. Administrators of both organisations sent out the initial invitation email to their members on behalf of the research team. Stroke physicians (defined as any physician involved in stroke care) and stroke nurses currently employed with NHS stroke clinical services were eligible to participate. Recipients were also asked to forward the survey details to any relevant Allied Health Professional groups they were connected to. Initial contact was through BASP or NSNF with email addresses provided to the research team by participants after round one. Subsequent contact with participants was then from the research team directly for round 2. We aimed to achieve broad geographical and professional coverage.

Questionnaire

The options were based on previous findings from our qualitative study [16] and discussion amongst the research team. Demographic data was collected including age, clinical role and years of experience in that role. The survey was case-based and asked participants to rate the extent that they approved or disapproved of 10 potential actions that could be carried out in common clinical scenarios occurring at the six-month clinic review (see Table 1). Although the options remained the same in each case, the clinical scenario content would vary. The scenarios were informed by previous work and generated through discussion amongst the research team which consists of General Practitioners (ET and LR), a senior stroke clinician (CP) and two researchers with experience of working in stroke and mental health using qualitative and preference elicitation approaches (CE and DF). The first three scenarios looked at issues related to the stroke-survivor themselves e.g. in general, for the young stroke-survivor and severity of the stroke. The final two scenarios incorporated the concept of risk assessment for dementia [17, 18] to assess whether use of such a tool would change clinical priorities. The scenarios described use of a tool which could identify an individual being at high or low risk of a future dementia. Participants were asked to use their judgement to consider the availability, practicality and cost effectiveness of each option. The survey was distributed via the Online Surveys platform (www.onlinesurveys.ac.uk).

Data collection

In the first Delphi round participants were presented with five clinical scenarios (see Table 1) and asked to assign ratings using a 7-point Likert scale (from very strongly disapprove to very strongly approve) to each of the ten options. Participants were also given an opportunity to provide free text comments. The overall rating assigned to each statement in round one was dependent on the median and interquartile range (IQR). If the statement had the same median and IQR they were ranked according to the total percentage of individuals who approved, quite strongly approved or very strongly approved the option. Finally, if any statements were still

Table 1 Clinical Scenarios and Available Actions to be Ranked

Clinical Scenarios Presented to Each Delphi Participant in Round 1	Clinical Actions to be Ranked For Each Scenario
CASE 1: Please prioritise the following actions for all stroke-survivors presenting with new post-stroke cognitive deficits reported at their six month review	Access to psychological services Additional communication with the GP Cognitive screen e.g. MoCA during six-month stroke clinic review Direct access to memory clinic services Ensuring allied health professional community follow-up e.g. occupational therapist for additional follow-up review in the community Ensuring compliance to secondary prevention is in place Follow-up in stroke-services GP to perform cognitive screen following discharge from specialist services Screening for a mood disorder Signposting individuals to other sources of information e.g. Stroke Association
CASE 2: Please prioritise the following actions for young stroke-survivors (under the age of 60) who are currently working presenting with new post-stroke cognitive deficits at their six-month review	
CASE 3: Please prioritise the following actions for stroke-survivors presenting with new post-stroke cognitive deficits after a severe stroke resulting in dependence on others at their six-month review.	
CASE 4: Please consider the following scenario. A 72 year stroke-survivor who presents with new subjective memory complaints. On further assessment using a risk prediction tool, she was found to be at high risk of developing cognitive failure/dementia in the next 2 years. Please prioritise the actions below based on this scenario.	
CASE 5: Please consider the following scenario. A 67 year stroke-survivor who presents with new subjective memory complaints. On a screening assessment using a risk prediction tool, he was found to be at low risk of developing cognitive failure/dementia in the next 2 years. Please prioritise the actions below based on this scenario.	

equal ranked after applying these first two criteria, the percentage of those who very strongly approved was used as the deciding factor for ranking. After round one, panellists were informed of summary statistics including aggregate median and the options were presented in rank order. Each participant was also reminded of the individual ratings they had given to all the options in the previous round and their free text comments.

Following discussions amongst the research team, given the consistent levels of approval ratings across the clinical scenarios for each statement in round one, a ranking exercise approach was then used to gain the final overall prioritisation for each statement. Participants were asked to rank the 10 options from 1 (most important) to 10 (least important) for each scenario. The overall ranking in round two was based on a points system for each rank. For example, 10 points were allocated for the statement ranked first (most important), 9 points for the statement for the second ranked statement and so on. The points for each statement in each scenario were then totalled and the ranking of each statement in each scenario was determined by the overall score from all respondents.

For each round, we allowed 2 weeks for participants to respond before a reminder was sent out with an additional week given to complete the survey before the survey was closed.

Data analysis

In line with other studies, consensus was defined as achieved if there was ≥75% agreement of all replies to a statement that fell within three categories (approve, quite or very strongly approve or disapprove) on the Likert scale [19–21]. The data was transferred and analysed using *Excel and STATA 15/16.*

Results

Round one

The demographics of the panellists that participated in round one is described in Table 2. In total there were 45 individuals, the majority were female (68.9%). There was representation from stroke physicians (44.4%; including neurologists), stroke nurses (46.7%; including specialist nurses (n = 13), stroke nurse (n = 6), stroke research nurse (n = 1) and stroke nurse practitioner (n = 1)) and allied health professionals (8.9%; including speech and language therapist, occupational therapists and physiotherapist). There was representation from most areas of the UK, except for East of England in round 1. The majority of participants in round one also reported that they performed six-month reviews (64.4%). Consensus was agreed to approve the majority of the statements in each clinical scenario (see Table 3). The only statement that consistently did not meet the consensus approval benchmark for the majority of the clinical scenarios was "GP to perform cognitive screen following discharge from specialist services". Responses in detail can be found in the online supplementary Table 1.

Round two

The demographics of round two participants are described in Table 2. Out of the 45 participants, 43 participants provided an email address to be contacted again for round two. Out of the 43, there were 21 eligible responses including stroke nurses (stroke nurse practitioner (n = 1), stroke nurse (n = 1), stroke specialist

Table 2 Demographics of Participants

	Round 1 (***n*** = 45) (n (%))	Round 2 (***n*** = 21) (n (%))
Age		
21–30	3 (6.7)	0 (0)
31–40	10 (22.2)	4 (19.1)
41–50	16 (35.6)	9 (42.9)
51–60	10 (22.2)	3 (14.3)
61–70	6 (13.3)	5 (23.8)
Gender		
Female	31 (68.9)	15 (71.4)
Male	13 (28.9)	6 (28.6)
Prefer not to say	1 (2.2)	0 (0)
Geographical Area		
East Midlands	2 (4.4)	2 (9.5)
Isle of Man	1 (2.2)	1 (4.8)
Isle of Wight	1 (2.2)	0 (0)
London	2 (4.4)	1 (4.8)
North East England	6 (13.3)	3 (14.3)
North West England	2 (4.4)	0 (0)
Oxford/Thames Valley	1 (2.2)	0 (0)
Scotland	7 (15.6)	3 (14.3)
South East England	6 (13.3)	1 (4.8)
South West England	6 (13.3)	3 (14.3)
Wales	3 (6.7)	2 (9.5)
West Midlands	5 (11.1)	3 (14.3)
Yorkshire and the Humber	3 (6.7)	2 (9.5)
Years of Experience		
0–5 years	13 (28.9)	1 (4.8)
6–10 years	9 (20.0)	6 (28.6)
11 or more years	23 (51.1)	14 (66.7)
Role		
Physician	20 (44.4)	12 (57.1)
Allied Health Professional	4 (8.9)	2 (9.5)
Nurse	21 (46.7)	7 (33.3)
Currently Performs Six-Month Review		
No	16 (35.6)	10 (47.6)
Yes	29 (64.4)	11 (52.4)

nurse ($n = 5$)). There was good geographical coverage with a mixture of participants from all three clinical groups represented, although there were more physician responses (57.1%). Approximately half of the participants conducted six-month stroke reviews (52.4%).

Table 4 describes the ranking of the actions in each case in both rounds 1 and 2. When it came to prioritising actions for stroke-survivors (including young stroke-survivors and also those with severe stroke resulting in dependence) presenting with cognitive difficulties, panellists felt that screening for a mood disorder was consistently a high priority across all three scenarios. Review by allied health professional in the community was also felt to be important to stroke-survivors presenting with cognitive deficits, again irrespective of the age or severity of problems. Finally, access to psychological services was important particularly for the young stroke survivor with cognitive deficits. There was limited agreement on the

Table 3 Summary Statistics Approval Ratings of Round 1

Statement	Case 1		Case 2		Case 3		Case 4		Case 5	
	Median (IQR)	% Approval and Above	Median (IQR)	% Approval and Above	Median (IQR)	% Approval and Above	Median (IQR)	% Approval and Above	Median (IQR)	% Approval and Above
Access to psychological services	7 (2)	91.1	7 (0)	97.8	5 (1)	82.2	6 (2)	95.6	5 (2)	64.4
Additional communication with the GP	6 (1)	84.4	6 (2)	91.1	5 (2)	84.4	6 (2)	93.3	5 (1)	80.0
Cognitive screen e.g. MoCA during six-month stroke clinic review	5 (2)	75.6	6 (2)	80.0	5 (2)	62.2	6 (1)	91.1	5 (2)	80.0
Direct access to memory clinic services	5 (1)	82.2	5 (2)	80.0	5 (2)	66.7	7 (1)	91.1	5 (2)	55.6
Ensuring allied health professional community follow-up e.g. occupational therapist for additional follow-up review in the community	6 (2)	86.7	7 (1)	91.1	6 (2)	88.9	6 (2)	84.4	5 (2)å	60.0
Ensuring compliance to secondary prevention is in place	6 (2)	91.1	7 (1)	97.8	6 (2)	93.3	7 (1)	97.8	6 (2)	93.3
Follow-up in stroke-services	6 (2)	77.8	6 (2)	88.9	6 (3)	68.9	5 (2)	71.1	5 (2)	66.7
GP to perform cognitive screen following discharge from specialist services	4 (1)	46.7	5 (1)	55.6	4 (1)	46.7	5 (1)	75.6	5 (1)	68.9
Screening for a mood disorder	6 (2)	95.6	7 (1)	97.8	6 (2)	95.6	6 (1)	100.0	6 (2)	93.3
Signposting individuals to other sources of information e.g. Stroke Association	7 (1)	97.8	7 (1)	97.8	7 (1)	95.6	6 (1)	95.6	6 (2)	95.6

Key: very strongly disapprove (1), quite strongly disapprove (2), disapprove (3), neutral (4), approve (5), quite strongly approve (6), very strongly approve (7)

Table 4 Ranking of Each Statement by Case in Rounds 1 and 2

Statement	Case 1		Case 2		Case 3		Case 4		Case 5	
	Round 1	Round 2	Round 1	Round 2	Round 1	Round 2	Round 1	Round 2	Round 1	Round 2
Access to psychological services	2	1	1	1	6	4	6	5	8	7
Additional communication with the GP	3	4	6	8	7	7	7	6	4	6
Cognitive screen e.g. MoCA during six-month stroke clinic review	9	6	8	4	9	8	5	2	6	4
Direct access to memory clinic services	8	8	10	9	8	9	2	1	10	10
Ensuring allied health professional community follow-up e.g. occupational therapist for additional follow-up review in the community	6	3	5	2	4	1	8	7	9	8
Ensuring compliance to secondary prevention is in place	5	9	4	6	3	6	1	3	2	3
Follow-up in stroke-services	7	7	7	5	5	3	10	9	7	5
GP to perform cognitive screen following discharge from specialist services	10	10	9	10	10	10	9	10	5	9
Screening for a mood disorder	4	2	3	3	2	2	3	4	3	1
Signposting individuals to other sources of information e.g. Stroke Association	1	5	2	7	1	5	4	8	1	2

role of primary care, as the proposal for General Practitioner's (GPs) to perform cognitive screening was ranked consistently low across all scenarios presented to the panellists. Direct access to memory clinic services was ranked consistently low across the first three scenarios. Although additional follow-up in stroke services was not generally approved across the scenarios, it was approved as a top three action for those with severe stroke and cognitive difficulties.

In the scenarios where a risk assessment for dementia was applied, irrespective of whether the individual was at high or low risk, respondents felt that screening for a mood disorder and compliance with secondary prevention were important. Unlike the previous scenarios, if an individual was found to be at high risk then direct access to memory clinics and a cognitive screen at the six-month review were felt to be important actions. Responses in detail can be found in the online supplementary Table 2.

Discussion

It is recommended that all stroke survivors receive a six-month review including a cognitive assessment, but there is no standardisation of content for general or specific patient groups. This exploratory electronic Delphi exercise by practicing National Health Service stroke clinicians and nurses describes priorities for actions at the six-month review. Irrespective of age and severity of stroke, there was agreement that actions should include screening for a mood disorder, ensuring allied health professional follow-up and access to psychology. It remains unclear which service should provide ongoing care as follow-up in stroke services was inconsistently approved and GP input in the form of cognitive assessment was consistently disapproved. However, direct access to memory clinics was approved if a risk assessment tool was used to identify individuals that were at high risk of developing dementia. This might reflect clinicians' views that earlier intervention delays or even reduces future cognitive decline, and that patients and carers have specialist information and support needs that cannot be met by standard stroke services.

Strengths and limitations

We captured the opinions of professionals involved in stroke care across the UK and professional groups but recognise several limitations. Although the response options available were generated and informed through discussion within an experienced research team and based on evidence from our previous work, only limited options were available to the participants to rank in each round. The fact that we were able to achieve high levels of consensus in round one suggests participants felt that these actions were not controversial, though different views may have been obtained by suggesting other aspects of care. We also recognise that the respondent numbers were small in comparison to the overall BASP and NSNF membership, and there was no similar society used to contact other AHPs. Further, we did not seek the opinions of GPs themselves and what their role would be in the management of stroke patients with cognitive impairments. However, we wished to focus on the six-month review and the majority of respondents had first-hand experience to guide their views about priorities during patient care at this time interval. We do appreciate that other professionals are involved in the six-month review, whom are not represented in this sample. This spread was limited by the member organisations we approached but we did still find that over half of the participants in each round conducted the six-month review. However, over 50% of participants in round one had 11 or more years of clinical experience with around two thirds of participants in round two having 11 or more years of clinical experience. This is important because a Delphi survey looks to seek consensus opinion from a group of experts [22], which we believe has been obtained here in spite of the relatively modest numbers who responded. Further, given the high level of consensus in round one it would seem unlikely that an alternative pattern would have been found amongst larger numbers of respondents. We do recognise that the use of only two rounds limited the conclusions to the strongest agreement only. Additional rounds would be needed to understand movement across final lower rankings and confirm the stability of the rankings. Further, the small number of respondents makes the data exploratory rather than definitive, and a larger study would be needed to confirm that the results are generalisable. We did not seek the opinions of other groups who would have greater assessment expertise in this area for example psychologists, as we wanted to capture the views from the clinicians involved in initially identifying issues amongst the wider stroke population. Mental health practitioners provide very detailed assessments to clarify exact nature of broader cognitive problems and do not perform the 6 month reviews. Where available, they receive referrals once an issue has been identified but there remains very inadequate provision of psychological services nationally, and if this professional group had been included it would have been difficult to interpret the data for implications across all services. Our project was exploring the initial step prior to their expert involvement as part of a wider holistic review.

Clinical implications

The results indicate that in line with national recommendations, professionals would value improvements in the care of patients with cognitive difficulties after

stroke. National Clinical Guidelines recommend routine review of cognition alongside assessment and management of mood during the rehabilitation phase post-stroke [9, 12]. The importance of cognitive care is recognised by professionals in this study but is not reflected in the way services are commissioned and provided. A Care Quality Commission Review in 2011 found that less than 40% of areas provided access to psychological therapy for all stroke-survivors regarding their cognitive difficulties [23]. Upon transfer home, the review also found that improvement was needed on the information supplied to stroke-survivors and carers regarding stroke-related cognitive problems such as memory and concentration [23]. An audit of longer term stroke services found that the longest delays in waiting times were found in accessing psychological support, particularly when compared with support for aspects of physical health e.g. physiotherapy [24]. This is in spite of recommendations that commissioning stroke services should be the same for physical care, rehabilitation as well as psychological care [25]. Six-month reviews enable clinicians and stroke patients to highlight these post-stroke cognitive deficits. However, there are still a number of areas where 6 month reviews are not being consistently performed [24]. This limits the opportunities for stroke patients and carers to present to their clinical provider with the more silent symptoms post-stroke such as cognition and subsequently accessing help in this area. Further, it is not quite clear who should be providing long-term care for post-stroke cognitive deficits.

Our study found that when considering the actions required at the 6-month review, clinicians believe that access to psychology is a key part of ongoing care in the general stroke population (case 1) and the young stroke-survivors (case 2). The role of primary care for cognitive assessment was generally not agreed. Currently, it seems that this gap in specialist psychological services may be met by staff in non-psychology disciplines (e.g. occupational therapists) who have voiced concerns about growing responsibilities associated with psychological assessments and the lack of necessary skills and training in this area [26]. If psychological services remain inconsistent across areas, then suitable alternative options should be found. An example of one in-patient initiative involved a "skill mix model" in order to maximise the resources available to the service and meet patient needs [27] by stratifying clinical psychology support at different levels of intervention [27]. In future, this may well also involve upskilling community psychology services or training other non-psychology disciplines within stroke care.

Memory clinics could potentially be an area where patients are followed up particularly if they demonstrate significant cognitive deficits post-stroke but their role is unclear. Although direct access was generally not approved across scenarios, this opinion seemed to change when we also sought the views of clinicians on actions if a risk assessment procedure was used in a patient reporting subjective memory complaints. Risk assessment in dementia is well researched with a number of tools developed to predict future dementia in the general population [17, 18]. Some have also been developed for stroke populations for post-stroke cognitive impairment [28] and dementia [29]. However, none are currently used in clinical care as few models have been externally validated. If this approach were to be used in the context of stroke in the future, then direct access to memory clinics for those at high risk of a future dementia illness appears to be supported by clinicians in stroke services. However, memory clinics vary in terms of staffing levels and follow-up processes [30], and it is unclear whether memory clinic services would be able to manage this additional workload. Further, although the majority are able to see new patients within 6 weeks, other memory assessment service users can wait on average over 12 weeks [30]. It may not be cost-effective to refer every stroke patient with cognitive difficulties into a memory assessment service based on a single screening assessment. By ensuring access to services outside of clinical stroke care, it may be possible to address inadequacies in specialist care [16], but this must be balanced against the burden placed upon memory assessment services and the views of stroke-survivors and their families when using a risk assessment approach [31].

Compliance with secondary prevention was highly ranked by participants when discussing management of those stratified into high and low risk categories via risk assessment tools. However, trial evidence about the impact on cognition has been mixed. When patients with recent stroke had intensive blood pressure and lipid lowering management there was no alteration in cognition at 2 years [32]. Active blood pressure treatment has previously been found to reduce risks of dementia and cognitive decline, but this was also associated with recurrent stroke with no clear effect on either dementia or cognitive decline has been found in the absence of recurrent stroke [33]. If future evidence supports specific secondary prevention measures then it is useful to understand that clinicians would support implementation.

Conclusions

This exploratory Delphi study has described consensus for actions by clinicians at the six-month review of stroke-survivors presenting with cognitive difficulties in

various contexts. There was strong support by participants in this study for improved specialist psychological support to be made available for patients. Stratification towards specialist memory services would be supported through use of risk assessment tools but further work is needed to assess the feasibility and cost-effectiveness of this approach.

Supplementary information

Supplementary information accompanies this paper at https://doi.org/10.1186/s12913-020-05558-y.

Additional file 1. Online Supplementary Table 1: Overall Responses from Round 1.

Additional file 2. Online Supplementary Table 2: Overall Responses from Round 2.

Abbreviations

BASP: British association of stroke physicians; GP: General practitioner; IQR: Interquartile range; NSNF: National stroke nursing forum; UK: United Kingdom

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Authors' contributions

ET conceived the framework for this study. ET collected, analysed and interpreted the data. ET prepared the manuscript for submission. LR helped to conceive the framework for this study and critically reviewed and edited the manuscript. CE helped to conceive the framework for this study and also critically reviewed and edited the manuscript. DF assisted with analysis of the data and critically reviewed and edited the manuscript. BS helped to conceive the framework for this study and critically reviewed and edited the manuscript. CP helped to conceive the framework for this study, assisted with analysis of the data and critically reviewed and edited the manuscript. The author (s) read and approved the final manuscript.

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Availability of data and materials

No further data will be made available.

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This study received ethical approval from the Newcastle University's Faculty of Medical Sciences ethics committee (1673/10898/2018). Consent via the online survey platform was obtained from each participant.

Consent for publication

Participants agreed to the publication of their research data but there are no individual person's data in any form.

Competing interests

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Publisher's Note

Online Supplementary Table 1: Overall Responses from Round 1

	Aggregated responses from round 1 n (%)						
Case 1: Statement	**very strongly disapprove (1)**	**quite strongly disapprove (2)**	**Disapprove (3)**	**Neutral (4)**	**Approve (5)**	**quite strongly approve (6)**	**very strongly approve (7)**
Signposting individuals to other sources of information e.g. Stroke Association	0	0	0	1 (2)	8 (18)	13 (29)	23 (51)
Access to psychological services	0	1 (2)	1 (2)	2 (4)	9 (20)	7 (16)	25 (56)
Additional communication with the GP	0	0	0	7 (16)	15 (33)	13 (29)	10 (22)
Screening for a mood disorder	0	0	0	2 (4)	11 (24)	10 (22)	22 (49)
Ensuring compliance to secondary prevention is in place	0	0	0	4 (9)	9 (20)	10 (22)	22 (49)
Ensuring allied health professional community	0	0	1 (2)	5 (11)	9 (20)	11 (24)	19 (42)

follow-up e.g. occupational therapist for additional follow-up review in the community							
Follow-up in stroke-services	1 (2)	1 (2)	2 (4)	6 (13)	6 (13)	12 (27)	17 (38)
Direct access to memory clinic services	0	0	2 (4)	6 (13)	17 (38)	11 (24)	9 (20)
Cognitive screen e.g. MoCA during six-month stroke clinic review	1 (2)	0	2 (4)	8 (18)	12 (27)	5 (11)	17 (38)
GP to perform cognitive screen following discharge from specialist services	3 (7)	2 (4)	4 (9)	15 (33)	12 (27)	7 (16)	2 (4)
Case 2: Statement							
Access to psychological services	0	1 (2)	0	0	5 (11)	4 (9)	35 (78)
Signposting individuals to other sources	0	0	0	1 (2)	5 (11)	9 (20)	30 (67)

of information e.g. Stroke Association							
Screening for a mood disorder	0	0	0	1 (2)	9 (20)	6 (13)	29 (64)
Ensuring compliance to secondary prevention is in place	0	0	0	1 (2)	9 (20)	9 (20)	26 (58)
Ensuring allied health professional community follow-up e.g. occupational therapist for additional follow-up review in the community	1 (2)	0	0	3 (7)	5 (11)	10 (22)	26 (58)
Additional communication with the GP	0	0	0	4 (9)	14 (31)	9 (20)	18 (40)
Follow-up in stroke-services	0	1 (2)	1 (2)	3 (7)	8 (18)	11 (24)	21 (47)
Cognitive screen e.g. MoCA during six-month stroke clinic review	1 (2)	0	2 (4)	6 (13)	6 (13)	8 (18)	22 (49)
GP to perform	1 (2)	3 (7)	3 (7)	13 (29)	16 (36)	3 (7)	6 (13)

cognitive screen following discharge from specialist services							
Direct access to memory clinic services	1 (2)	0	1 (2)	7 (16)	16 (36)	7 (16)	13 (29)
Case 3: Statement							
Signposting individuals to other sources of information e.g. Stroke Association	0	0	0	2 (4)	9 (20)	11 (24)	23 (51)
Screening for a mood disorder	0	0	0	2 (4)	12 (27)	9 (20)	22 (49)
Ensuring compliance to secondary prevention is in place	0	0	1 (2)	2 (4)	11 (24)	12 (27)	19 (42)
Ensuring allied health professional community follow-up e.g. occupational therapist for additional	0	0	1 (2)	4 (9)	11 (24)	9 (20)	20 (44)

follow-up review in the community							
Follow-up in stroke-services	0	3 (7)	3 (7)	8 (18)	7 (16)	10 (22)	14 (31)
Access to psychological services	0	2 (4)	2 (4)	4 (9)	15 (33)	12 (27)	10 (22)
Additional communication with the GP	0	0	1 (2)	6 (13)	16 (36)	6 (13)	16 (36)
Direct access to memory clinic services	2 (4)	0	3 (7)	10 (2)	16 (36)	5 (11)	9 (20)
Cognitive screen e.g. MoCA during six-month stroke clinic review	1 (2)	1 (2)	1 (2)	14 (31)	6 (13)	11 (24)	11 (24)
GP to perform cognitive screen following discharge from specialist services	2 (4)	1 (2)	7 (16)	14 (31)	14 (31)	5 (11)	2 (4)
Case 4: Statement							
Ensuring compliance to secondary	0	0	0	1 (2)	6 (13)	12 (27)	26 (58)

prevention is in place							
Direct access to memory clinic services	0	0	0	4 (9)	6 (13)	12 (27)	23 (51)
Screening for a mood disorder	0	0	0	0	8 (18)	15 (33)	22 (49)
Signposting individuals to other sources of information e.g. Stroke Association	0	0	0	2 (4)	9 (20)	12 (27)	22 (49)
Cognitive screen e.g. MoCA during six-month stroke clinic review	0	1 (2)	1 (2)	2 (4)	7 (16)	12 (27)	22 (49)
Access to psychological services	0	0	0	2 (4)	12 (27)	10 (22)	21 (47)
Additional communication with the GP	0	0	1 (2)	2 (4)	10 (22)	11 (24)	21 (47)
Ensuring allied health professional community follow-up e.g. occupational	0	0	0	7 (16)	11 (24)	9 (20)	18 (40)

therapist for additional follow-up review in the community							
GP to perform cognitive screen following discharge from specialist services	1 (2)	1 (2)	2 (4)	7 (16)	13 (29)	12 (27)	9 (20)
Follow-up in stroke-services	1 (2)	1 (2)	3 (7)	8 (18)	10 (22)	11 (24)	11 (24)
Case 5: Statement							
Signposting individuals to other sources of information e.g. Stroke Association	0	0	0	2 (4)	13 (29)	9 (20)	21 (47)
Ensuring compliance to secondary prevention is in place	0	0	0	3 (7)	9 (20)	11 (24)	22 (49)
Screening for a mood disorder	0	0	0	3 (7)	14 (31)	14 (31)	14 (31)
Additional communicatio	0	0	0	9 (20)	20 (44)	10 (22)	6 (13)

n with the GP							
GP to perform cognitive screen following discharge from specialist services	1 (2)	1 (2)	4 (9)	8 (18)	26 (58)	2 (4)	3 (7)
Cognitive screen e.g. MoCA during six-month stroke clinic review	0	1 (2)	2 (4)	6 (13)	15 (33)	7 (16)	14 (31)
Follow-up in stroke-services	0	1 (2)	7 (16)	7 (16)	14 (31)	9 (20)	7 (16)
Access to psychological services	0	0	3 (7)	13 (29)	12 (27)	12 (27)	5 (11)
Ensuring allied health professional community follow-up e.g. occupational therapist for additional follow-up review in the community	0	0	2 (4)	16 (36)	9 (20)	7 (16)	11 (24)

Direct access to memory clinic services	0	0	4 (9)	16 (36)	13 (29)	10 (22)	2 (4)

Online Supplementary Table 2: Overall Responses from Round 2

Case 1	Total	Case 2	Total	Case 3	Total	Case 4	Total	Case 5	Total
Access to psychological services	154	Access to psychological services	162	Ensuring allied health professional community follow-up e.g. occupational therapist for additional follow-up review in the community	155	Direct access to memory clinic services	151	Screening for a mood disorder	160
Screening for a mood disorder	145	Ensuring allied health professional community follow-up e.g. occupational therapist for additional follow-up	147	Screening for a mood disorder	146	Cognitive screen e.g. MoCA during six-month stroke clinic review	149	Signposting individuals to other sources of information e.g. Stroke Association	154

		review in the community							
Ensuring allied health professional community follow-up e.g. occupational therapist for additional follow-up review in the community	129	Screening for a mood disorder	144	Follow-up in stroke-services	143	Ensuring compliance to secondary prevention is in place	143	Ensuring compliance to secondary prevention is in place	142
Additional communication with the GP	122	Cognitive screen e.g. MoCA during six-month stroke clinic review	119	Access to psychological services	125	Screening for a mood disorder	139	Cognitive screen e.g. MoCA during six-month stroke clinic review	116
Signpostin g individuals to other sources of informatio	115	Follow-up in stroke-services	117	Signpostin g individuals to other sources of informatio	117	Access to psychological services	122	Follow-up in stroke-services	112

n e.g. Stroke Association				n e.g. Stroke Association					
Cognitive screen e.g. MoCA during six-month stroke clinic review	110	Ensuring compliance to secondary prevention is in place	115	Ensuring compliance to secondary prevention is in place	115	Additional communication with the GP	104	Additional communication with the GP	109
Follow-up in stroke-services	107	Signposting individuals to other sources of information e.g. Stroke Association	108	Additional communication with the GP	105	Ensuring allied health professional community follow-up e.g. occupational therapist for additional follow-up review in the community	98	Access to psychological services	100
Direct access to memory clinic services	106	Additional communication with the GP	99	Cognitive screen e.g. MoCA during six-month stroke	96	Signposting individuals to other sources of informatio	91	Ensuring allied health professional community	99

				clinic review		n e.g. Stroke Association		follow-up e.g. occupational therapist for additional follow-up review in the community	
Ensuring compliance to secondary prevention is in place	104	Direct access to memory clinic services	73	Direct access to memory clinic services	94	Follow-up in stroke-services	80	GP to perform cognitive screen following discharge from specialist services	87
GP to perform cognitive screen following discharge from specialist services	63	GP to perform cognitive screen following discharge from specialist services	71	GP to perform cognitive screen following discharge from specialist services	59	GP to perform cognitive screen following discharge from specialist services	78	Direct access to memory clinic services	76

7.3.1 PP7 Commentary

In this national Delphi survey of stroke healthcare professionals' views, we were able to reach consensus on the majority of statements after round one, perhaps a reflection on the need for further emphasis by stroke clinicians on cognitive difficulties post-stroke. The main findings from the study for stroke-survivors with cognitive problems include the following: 1) Access to psychological services is important particularly for young stroke-survivors 2) Allied health professional follow-up was felt to be important and should be prioritised in the community 3) Screening for a mood disorder is important. Across different scenarios exploring risk assessment, there were different views about priorities according to the information presented. Specifically, for those deemed to be at high risk, it was felt that direct access to memory clinic services would be helpful and those at lower risk more conservative measures needed to be adopted such as screening for a mood disorder and signposting individuals to further information. Interestingly throughout the scenarios, cognitive screening by a GP was ranked consistently as a low priority. Similarly, unless they were young stroke patients, cognitive screening at the six-month review was generally not approved. This was unless a risk assessment tool was involved where it was then ranked in the top 4 actions overall for high and low-risk outcomes.

The report by NHS Improvement on "Psychological Care after stroke" highlighted the need for clear pathways for referral to either neuropsychology or clinical psychology when assessing cognition, with a fast track route for urgent support if needed (Gillham and Clark, 2011). The six week and six month review should be used to monitor changes (Gillham and Clark, 2011). There is a lack of psychological services on offer to patients as evidenced from the most recent SSNAP report (Sentinel Stroke National Audit Programme, 2020). In 2011, the Care Quality Commission conducted the "Supporting Life After Stroke" review of stroke services (Care Quality Commission, 2011). Neuropsychology (regarding cognitive difficulties) and psychological therapy were amongst the lowest readily available forms of support reported by primary care trusts, with less than 40% of areas providing good access (Care Quality Commission, 2011). This gap in provision will unfortunately result in more people not receiving the support they need although more research is needed to identify an evidence-based intervention specific for cognitive issues post-stroke. It may also mean that as these cognitive deficits are not picked up initially, if they become apparent as physical recovery progresses or they

develop into a dementia illness, diagnosis will be delayed. It is therefore not surprising that clinicians in this Delphi study would strongly advocate access to psychological care.

Clinicians surveyed also valued allied health professional follow-up in the community. In the Care Quality Commission report, there was good availability in all if not most parts for services such as speech and language therapy, occupational therapy and general physiotherapy (Care Quality Commission, 2011). This again highlights that the main focus in stroke rehabilitation has been on physical recovery. However, participants in this study felt that more allied health professional help is required in the context of cognitive issues following a stroke. Although we did not specify which allied health professional would be most helpful, occupational therapists do aim to ensure maximum levels of function and independence in life post-stroke (Legg et al., 2006). This will of course include an assessment of cognitive function as cognitive impairment post-stroke can limit independence during activities of daily living (Zinn et al., 2004). However, a previous systematic review assessing the effectiveness of occupational therapy for post-stroke cognitive impairment only identified one trial , and advised more research was needed because the study population was small in this trial (Hoffmann et al., 2010). Given the current lack of evidence for supplementary occupational therapist intervention, it is therefore important to understand which allied health professional would be able to undertake the most effective assessment and response in the community.

Participants emphasised the need for mood to be screened for those with post-stroke cognitive difficulties. Around 31% stroke-survivors develop depression following a stroke (Hackett and Pickles, 2014). This is important as around half of the patients who have a major depressive disorder can also have generalised cognitive impairment (Kohler et al., 2010). In fact, cognitive impairment has been found to be a consistent predictor of post-stroke depression (Towfighi et al., 2017). There have been recommendations that cognition and mood disorders should be screened at different stages along the stroke assessment pathway from acute assessment to outpatient clinic and beyond (Quinn et al., 2018). Despite this, cognitive screening by GPs was not favoured by participants nor was it approved for patients presenting with cognitive complaints unless they were young or when a risk assessment procedure has been carried out. With regards to the consistent disapproval for GP's to do cognitive screens, future research should examine why this might be the case

and what alternatives there might be to determine the role of the GP, particularly as stroke services end at the 6-month review. As Quinn et al have proposed, dementia should not be diagnosed till at least six months post-stroke (Quinn et al., 2018) and patients need to have a clear contact point in order for such an assessment to be made. This might be where risk assessment tools could prove to be useful for determining the direction of follow-up care. The high-risk patients could be directed to a specialist memory clinic and those at low risk could continue to be monitored in primary care. If this decision is made during the six-month review, then this would ensure that patients developing a future dementia illness are not left without support. The difficulty would be the additional work this generates for memory clinics and whether they have the capacity to take on this additional at-risk population.

7.4 Chapter Summary

In this chapter some guidance has been provided for the management of cognitive issues after stroke from a national panel of experts. Participants have highlighted the need for more psychological service input which is already a recognised challenge for stroke services. Risk prediction tools on their own, as evidenced in chapter 6, can lead to concerns about the benefits of a service response, but participants highlighted a possible different direction for both high and low risk scenarios. Risk assessment tools can also emphasise to the clinician the need for cognitive assessment. The next step is to be able to produce a risk assessment tool which can accurately discriminate between high and low risk stroke cases for dementia.

Chapter 8. Discussion

In this chapter I bring together the findings from the seven published papers presented in this thesis. A short commentary following each paper in the previous chapters has already been provided. For this final chapter I:

a) Present the principal findings of my published manuscripts in relation to the objectives set out in chapter 1;
b) Discuss the overall strengths and limitations of my findings;
c) Supplement the commentaries in the previous chapters by presenting these findings in relation to other similar work being conducted in this field;
d) Highlight the clinical implications of the principal findings of my thesis; and,
e) Discuss the future work needed along the clinical care spectrum of post-stroke dementia based on the work presented in this thesis.

8.1 Principal findings

The research findings have highlighted some key limitations in the current clinical care pathway in supporting stroke-survivors who may be at risk of a future dementia illness. The potential use of risk assessment tools to assist in the identification of individuals at risk of post-stroke dementia has also been explored.

The key findings in relation to the objectives are as follows:

Objective i): To describe the impact of cognitive difficulties post-stroke over time

Through a systematic review of the available literature (paper 1; (Tang et al., 2018a) patterns in post-stroke cognition were described by investigating changes in cognitive test scores over time. While most stroke survivors showed general cognitive decline, this was not found universally. Cognitive function post stroke could stabilise or even recover, and this was dependant on both the follow-up time and the cognitive domain examined. There were also variables associated with impairment which included age, ethnicity, premorbid cognitive performance, depression, stroke location and a history of stroke.

Objective ii): To describe the current care provision from the perspectives of patients, carers and key professionals

The findings from papers 2 – 4 ((Tang et al., 2017a, Tang et al., 2018c, Tang et al., 2020a) highlight the lived experience of stroke-survivors with memory difficulties as well as the experiences of their families. They also provide clinician perspectives on the care received by stroke-survivors with cognitive difficulties in general. During these interviews, stroke-survivors and their family carers discussed the physical and emotional impact that the stroke illness and the memory difficulties have had on their daily lives. They reported adaptations they made in order to continue to try and function in the community. However, they also expressed a number of difficulties in accessing the care they need due to both personal (fear of dementia and minimisation of symptoms) and organisational (barriers found in primary care services) factors. These service gaps were also acknowledged by primary and secondary care clinicians. Organisational (lack of clarity in service pathways and less focus on cognition in stroke care) and clinician-related (difficulties in discussing cognition and assumptions made in clinical care) factors were found to contribute to gaps in care for these patients.

Objective iii): To explore the use of risk prediction tools to identify those most at risk

Dementia risk prediction tools have primarily been developed and externally validated in the general population rather than in disease specific groups (e.g. people with stroke or cardiovascular disease). Paper 5 (Tang et al., 2020b) examines the performance of dementia risk prediction models developed for use in the whole population when applied to people with a history of stroke. However, the current dementia risk models do not perform well in stroke cohorts. Therefore, if this approach is to be used then stroke-specific models would need to be developed and then externally validated in stroke populations to ensure their accuracy, generalisability and transportability. As part of the qualitative interviews, clinicians, patients and their family carers were asked their thoughts about incorporating risk prediction models into the care of stroke-survivors (Tang et al., 2019). The opinions were mixed. From their accounts, although there might be benefits to this approach, it should not be applied universally due to concerns about the potential diagnosis of dementia, lack of intervention after assessment and how it may affect recovery. To

be told you are at risk of dementia having recovered well from your stroke could be concerning for some.

Objective iv): To seek the views of professionals on the key findings from the previous objectives with a view to suggesting improvements in future care.

An exploratory national electronic Delphi exercise was conducted focussing on priority actions at the six-month clinical review and how a dementia risk prediction tool could be incorporated into services. The main input that stroke clinicians wanted was the assistance of other healthcare professionals such as psychological services and enhanced allied health professional follow-up. Dementia risk prediction tools could be used to identify those at high risk who could possibly be redirected to memory clinics.

8.2 Strengths and limitations of the studies overall

The body of work presented in this thesis provides a comprehensive overview of the current care of stroke-survivors with memory difficulties and how interventions, such as risk prediction models, could be used in the clinical pathway to improve the identification and care of patients at highest risk of post-stroke dementia. The work involved a wide range of stakeholders such as primary and secondary clinicians (including allied health professionals) both locally and nationally (for secondary care professionals), and most importantly the views of patients and their families. There was also the opportunity to collaborate and learn from international colleagues to maximise the potential of multiple stroke datasets through harmonisation.

The external validation of dementia risk models in stroke cohorts is the first examination of harmonised datasets being used to determine whether existing dementia risk models validate well in people with a history of stroke. A previous paper has also highlighted the current methodological weaknesses in dementia risk prediction literature including the over-reliance on one data source and a lack of validation (Goerdten et al., 2019). The study externally validating these models in stroke cohorts adds further evidence in this field but also takes into account these weaknesses.

Throughout the research process patients and the public assisted in the development of the research materials used and provided feedback on the findings and dissemination strategies. Sufficient time was given, at least annually to listen to their feedback to improve the overall research programme; this was often the highlight of the PhD process. Arguably, the biggest strength has been to bring to the fore the "hidden" issues of memory and cognitive difficulties in stroke survivors to a wide ranging clinical and non-clinical audience. Often, research and clinical services focus on the physical recovery from stroke. This work highlights aspects of the recovery process that clinicians may not always identify themselves, despite the fact that they acknowledge its importance in the patient journey.

There are some limitations in the presented studies. For the systematic review, the focus was on the change and trajectory of cognitive test scores. This was because of existing systematic reviews on dementia outcome in relation to stroke (Kuzma et al., 2018, Savva and Stephan, 2010). However, cognitive test score deficits may not necessarily reflect the individual's ability to function or indeed their own perceived deficits. It is recognised that stroke-survivors could perform well on cognitive testing but then struggle to function and perform activities of daily living and vice versa. Therefore, although this body of work has increased our understanding on how patient's perform in terms of cognitive testing over time across cognitive domains, it does not provide evidence of how these cognitive deficits subsequently affect functioning. There also needs to be some consideration given to how perceptual and physical impairments may interact with cognitive deficits. Although this was in part supposed to be answered in the qualitative interviews, I also recognise that cognitive testing was not done in recruiting stroke-survivors to the interviews.

With regard to the qualitative studies, the inclusion criteria required only subjective memory concerns which meant in terms of the spectrum of cognitive deficits this somewhat limited in my sample. Patients may have had difficulties with attention, information processing or executive functioning but this was not clear from the participants recruited as there was no formal cognitive assessment. Additionally, it was not clear whether patients were referring to ongoing cognitive difficulties since their stroke, which they became more aware of since returning home, or whether this had commenced after their discharge from hospital. Further, as these were memory concerns reported by the patient, they may have had pre-morbid memory difficulties

which became more obvious following the stroke and were therefore not directly due to the stroke itself. Further, memory concerns are generally one of the most common cognitive deficits experienced and reported by stroke-survivors (Stroke Association, 2018b). In order to determine the effect of objective cognitive deficits on daily functioning, patients would need to be recruited following objective cognitive testing. This could be for example with a stroke specific cognitive test such as the Oxford Cognitive Screen which is freely available and takes into account stroke deficits such as aphasia and neglect (Demeyere et al., 2015). As evidenced by the systematic review, follow-up time is important with cognitive decline generally found with longer follow-up times. It would therefore be helpful to follow-up patients and their families over a longer period than the first 12 months post-stroke. A further limitation of the qualitative studies was that the patients recruited were mobile and well enough to attend the six-month clinic review. There will be those with more severe major stroke and not able to attend their review who may be more at-risk of dementia and may encounter even more significant daily difficulties who were not included in this study.

Although it was possible to harmonise a number of stroke datasets to externally validate the existing dementia risk models, this process has its limitations. The first involves the different definitions of the risk variables for example measures of depressive symptoms, alcohol consumption and education, across the different datasets. When utilising different datasets from varying geographical locations internationally this was to be expected. The second was the choice of dementia risk models chosen to be externally validated. For disease-specific models, disease-specific variables have been found to perform well in that population for example in diabetes specific dementia models (Exalto et al., 2013). However, there has only been one stroke-specific dementia model published (Lin et al., 2003). Further the stroke-specific variables include neuroimaging which may have been missing or been reported differently across cohorts, making harmonisation even more difficult. Accurate models where there were available data to harmonise across the different cohorts were chosen. As such, there may be other untested dementia risk models that work better in stroke populations. The likelihood of this is probably low as the variables found in the tested dementia risk assessment models tended to be vascular in origin such as blood pressure or cholesterol. An individual who has had a stroke illness would tend to score high on these variables anyway and so additional stroke-specific variables may be needed to provide additional accuracy to these traditionally used risk variables. Finally, although the size of the population was increased via

data harmonisation, the total samples that were harmonised were still relatively small when compared to some of the existing literature in external validation in dementia risk prediction (Stephan et al., 2020, Licher et al., 2018b, Exalto et al., 2013). However, by their very nature stroke cohorts tend to be smaller samples but it is recognised that more datasets might have provided better power for analysis of co-variates, but it was at the discretion of the individual studies as to whether they were permitted and willing to share their data.

The national electronic Delphi survey incorporated the views of stroke clinicians only. Primary care professionals are also involved in the care of stroke-survivors at risk of dementia. However, a definite clinical focus point in the service pathway was needed so this could be enhanced and improved upon particularly as the six-month reviews are routinely conducted due to national recommendations. This is why the study focussed on the six-month clinical review which is generally conducted in stroke outpatient services. There are some limitations to this approach. First, the majority of clinical care following a stroke is found in the community, which may or not be part of hospital with only limited contact with specialist stroke services following discharge. This means that if a long-term intervention was to be trialled it is likely that this will be most appropriately placed in the community. In terms of identifying those suspected of having a dementia diagnosis, GPs perform brief cognitive test scores alongside careful history and examination and appropriate investigations (Robinson et al., 2015). However, from this Delphi survey, having GPs perform cognitive testing post-discharge was generally the lowest ranked option across the scenarios. This presumably placing the onus on stroke services to carry out this assessment. This may reflect the traditional lack of primary care involvement in post-stroke care for example, in the latest periodic national audit of stroke six-month reviews, only 0.1% of six-month reviews were conducted by GPs, with only around 7 in 10 eligible stroke patients receiving mood, behaviour and cognition screening (Sentinel Stroke National Audit Programme, 2019b). However, only around a third of applicable stroke survivors receive a six-month review in current clinical care (Sentinel Stroke National Audit Programme, 2019c), which means there is a substantial number of stroke survivors who do not get follow-up long term care through stroke services. This is despite the fact that around three quarters of all stroke survivors are eligible for follow-up (Sentinel Stroke National Audit Programme, 2019c). This may or may not reflect the fact that many stroke patients have their high care needs met in 24-hour care, which means that they have sufficient monitoring in

the community. This highlights the importance of community follow-up which is through the GP. Second, although there was good geographical coverage of clinicians from the invitations sent out, the spectrum of those conducting six-month reviews was restricted to mainly physicians and nurses. In some areas, allied health professionals including staff employed by parties such as the Stroke Association conduct some of these six-month reviews and therefore it would have been useful to obtain more of their views. Finally, there may be other options besides the ones presented to participants to improve the care of those at-risk of dementia. However, the options were informed through discussion amongst the research team and also the previous work presented in this thesis.

8.3 Interpretation in relation to other studies

In the previous chapters, a brief commentary after each paper has been provided to place each study in the context of existing literature. This section will look to build upon this existing commentary and bring together the findings from the entire thesis in relation to the overall picture presented in the current literature.

Similar to paper 1 (Tang et al., 2018a), previous studies have looked at cognitive changes over time. This has been in relation to frequency of cognitive impairment (Sexton et al., 2019) or dementia (Kuzma et al., 2018) over time. These studies have confirmed the increased risk of cognitive impairment and dementia following a stroke, which is also what paper 1 concluded through cognitive testing. A more recent systematic scoping review by Saa and colleagues (Saa et al., 2019) has built on the systematic review (Tang et al., 2018a). Here, the authors looked at studies evaluating cognition longitudinally and identified the instruments and domains they used (Saa et al., 2019). Fourteen articles were included in my study, which looked at the frequency of for example those who decline cognitively, those who recover or stabilise. The study by Saa et all included 257 studies, which looked at the descriptive characteristics of included studies in detail for example the instruments used, domains tested and the use of functional cognitive assessments (Saa et al., 2019). The systematic review did not look at a specific group of stroke-survivors. This is in contrast to my own systematic review, which ensured that the population tested in my systematic review was dementia free at baseline. Further, the review looked at those who were older i.e. ≥50 years old; this was to provide a broader picture of those at risk of developing dementia from cognitive impairment particularly as age is a strong risk factor for dementia. Although the focus of Saa's review was on the

characteristics of the measures of cognitive over time, it was complimentary to the systematic review submitted in this thesis as it highlights the broad range of multi and domain specific tests currently used for both intervention trials and observational studies in the current literature. As per the study authors' conclusions, there also needs to be better organisation and standardisation in the field of cognitive testing to improve our understanding of cognitive trajectory post-stroke (Saa et al., 2019). However, it was then important to understand the actual impact on patients in order to know what interventions they may require which was the aim of the qualitative study.

The qualitative study focussed on subjective memory difficulties and concerns rather than any objective measures. It is known that new memory impairments are commonly found post-stroke and can occur even amongst patients with excellent clinical recovery (Jokinen et al., 2015). Further, older (i.e. aged 65 years and over) chronic stroke patients have been found to show significantly more impairment in cognitive domains such as executive functioning and verbal memory when compared to younger stroke patients (Nakling et al., 2017). Unfortunately, currently identified tools to measure subjective memory impairment in the literature do not provide an accurate reflection of memory impairments post-stroke (Salis et al., 2019). However, subjective memory impairment or complaints are known to be associated with future dementia (Brigola et al., 2015, Jessen et al., 2010, Schmand et al., 1996, Jonker et al., 2000) . Midlife forgetfulness also appears to be an indicator of increased dementia risk in old age (Ishtiak-Ahmed et al., 2019). It is known that self-reported concerns about worsening memory in patients with mild cognitive impairment is a predictor of future dementia (Wolfsgruber et al., 2014). It is therefore reasonable to clarify with the patient if they have experienced any memory concerns following their stroke in order to consider whether any further assessment is required for a future dementia illness through cognitive testing or even onward referral to memory clinics or further additional review in the community.

There have been numerous qualitative studies exploring the impact of stroke on stroke-survivors and caregivers as well as the organisation of services (McKevitt et al., 2004). The patient and family caregiver interviews were specifically targeted at those experiencing subjective memory complaints (Tang et al., 2018c) and the impact this had (Tang et al., 2020a). The study here adds to the qualitative literature for this specific at-risk stroke subgroup of stroke patients also reporting memory

concerns. The barriers identified in primary care however are not specific to this stroke subgroup. A recent systematic review of qualitative studies of stroke-survivors and their caregivers' experiences of primary care found that in general stroke survivors feel abandoned and marginalised by services (Pindus et al., 2018). It was noted that only a minority of studies included in this review included data on specific long term impairments such as cognitive impairment (Pindus et al., 2018). Some of the recommendations to address these negative perceptions included information provision and improving the continuity of care between specialist and generalist services (Pindus et al., 2018). These two facilitators of information provision and better integrated care were also found when healthcare professionals were interviewed in my study (Tang et al., 2017a). The focus of this thesis was not to develop interventions to alleviate the impact of subclinical cognitive difficulties. The purpose of this body of work was to show why patients at risk of post-stroke dementia and their families require more assessment and clinical intervention than they can access in standard services. This is particularly relevant because a proportion of these individuals will go on to develop a dementia illness. It is therefore important to know if we are able to identify these individuals earlier and whether stroke patients would value such an intervention. Risk assessment tools are one objective way to achieve this, but their cost effectiveness and ethical concerns around their use still need to be determined. Importantly, they require external validation to assess how transferable and generalisable they are in a population separate to the development cohort before they can be used.

Studies focussing on external validation of dementia risk models have been limited (Stephan et al., 2016). There have been previous papers externally validating dementia risk models (Exalto et al., 2014, Licher et al., 2018b, Stephan et al., 2020). A recent study by Stephan et al (Stephan et al., 2020), applied similar methods to the external validation study presented here and looked at the performance of some of the same models used (Tang et al., 2020b) namely the Cardiovascular Risk Factors, Aging and Dementia risk score, the Australian National University Alzheimer's Disease Risk index and the Brief Dementia Screening Indicator (Stephan et al., 2020). They tested the models in low-income and middle-income countries, as the dementia prediction models have generally been developed and tested in high income countries (Stephan et al., 2020). The authors found a mixed picture in terms of external validity when assessing the accuracies of these models in external populations, although the Australian National University Alzheimer's Disease Risk

index and the Brief Dementia Screening Indicator models did perform similarly to the development cohorts (Stephan et al., 2020). However, this was not tested in disease-specific populations as in the study presented in this thesis. Further, when Licher and colleagues externally validated the same three models in an elderly community-dwelling population, they found that all models were similar in discrimination when compared to prediction based on age alone (Licher et al., 2018b). These studies highlight the need for new and updated models to be developed as well as the need to look at disease-specific risk prediction models.

There has also been some risk prediction models developed in stroke populations to predict dementia (Lin et al., 2003) and post-stroke cognitive impairment (Chander et al., 2017, Kandiah et al., 2016, Ding et al., 2019). However, to our knowledge this is the first study to examine the performance of general population-based dementia risk prediction models in stroke populations. Multiple cohorts were also harmonised to increase the sizes of the samples used, which is a similar approach used by previous studies (Lipnicki et al., 2019, Lo et al., 2019). This is because when compared to general population cohorts, stroke cohorts in general are small hospital-based samples as evidenced by the numbers used to develop the stroke models (range n = 179 (Ding et al., 2019) – 283 (Lin et al., 2003)). The majority of stroke models are to predict post-stroke cognitive impairment whereas the focus of investigation is a dementia outcome. Further it was not possible to validate these stroke models due to limited and differing available variables across the cohorts I had access to. However, the study (Tang et al., 2020b) has further emphasised that stroke-specific dementia risk models are needed. Although the focus of the external validation study was on risk models that could be used in primary care, this limits the types of variables that can be incorporated into such models. Indeed, if blood based (or cerebrospinal fluid based) biomarkers and neuroimaging variables are to be incorporated into stroke-specific models this would mean that risk prediction models would have to be used in specialist settings to obtain the necessary variables. One area that has received considerable interest has been the use of neuroimaging variables, which were incorporated into both models developed for predicting post-stroke cognitive impairment (Chander et al., 2017, Kandiah et al., 2016).

In a systematic review of studies, global brain and medial temporal lobe atrophy have been found to be the most consistent predictors of post-stroke cognitive

impairment (Casolla et al., 2019). Predictors of a favourable cognitive outcome (i.e. normal cognitive function or mild cognitive impairment) post stroke in a study that looked at 7 years follow-up for those after first-ever stroke or TIA included lower medial temporal lobe atrophy grade on MRI (Hagberg et al., 2019). Other potential imaging variables that have been associated with the development of dementia in stroke patients include imaging markers of severe small vessel disease (i.e. presence of ≥3 lacunes and confluent white matter changes) (Mok et al., 2016) and leucoaraiosis (Pendlebury and Rothwell, 2019). Stroke subtype may also be important as a higher number of cerebral microbleeds, higher cortical atrophy score and disseminated superficial siderosis have been found to be risk factors for new-onset dementia in those who have a stroke due to intracerebral haemorrhages (Moulin et al., 2016). In terms of blood biomarkers, there is currently no convincing biomarker (including APO e4, cholesterol, C-reactive protein, glycated haemoglobin A1c and homocysteine) which can accurately diagnose or predict post-stroke cognitive impairment (Casolla et al., 2019). There have been some studies for example using plasma D-amino acid oxidase (Chen et al., 2019b), which have been associated with PSD that need further exploration but at present there are no effective blood biomarkers for PSD (Mijajlovic et al., 2017). Based on current data, it is possible that neuroimaging variables could assist in the development of more accurate stroke-specific dementia risk models, which could be of use in specialist settings. An initial simpler, stroke-specific community screen could also be considered prior to specialist setting involvement to further stratify these individuals.

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The qualitative study also provides important insights about the views of stakeholders, including stroke survivors, about dementia risk assessment (Tang et al., 2019). Previous studies have sought the views of clinicians on the use of risk prediction models in general (Muller-Riemenschneider et al., 2010, Sarazin et al., 2013) and also in disease-specific settings (Liew et al., 2013). In dementia, a survey of primary care professionals found that participants agreed that risk prediction models could be helpful in practice (Tang et al., 2018b). When members of the public were asked for their views on risk assessment in dementia, there was a preference for this to be embedded within routine health checks. However, participants also felt it important as they considered this a complex area comprising a range of approaches including case finding and genetic screening (Robinson et al., 2018). This qualitative study for stroke patients therefore adds to the existing literature as it specifically addresses the question as to whether risk assessment tools for dementia would be

suitable for a stroke population. In my study, with risk assessment in general, understanding individual preferences is key. Similarly participants in the study by Robinson et al also discussed the negative psychological consequences of proactive approaches for example not wanting to know because of their personal experiences of seeing others with dementia or worrying about future dementia when they are asymptomatic (Robinson et al., 2018). With such concerns, it was important to know how to incorporate these findings into clinical practice. One way to possibly achieve this was to seek expert consensus opinion on how to improve the six-month review, which is dictated by national policy and expert guidance. This was the stroke six-month review. The findings of the previous studies were brought together in a Delphi survey and the opinions of experts in the UK were sought.

The Delphi survey specifically focused on management of cognitive problems at the six-month clinic review. Previous studies around the six-month clinic review concentrated on the assessment tools used (Patchwood et al., 2020) and the purpose and outcomes of the review (Abrahamson and Wilson, 2019a). A recent study looked at whether unmet needs post-stroke were addressed by the six-month review but the focus was on physical needs, secondary prevention and self-management (Abrahamson and Wilson, 2019b). There has been little focus on the cognitive aspects of care at this clinical review. This study has therefore been able to provide evidence as to what could be valuable from a cognitive perspective and could be incorporated into routine clinical practice. For example, it was clear from the participants in this study that GPs performing cognitive assessments post-discharge was not favoured (Tang et al., 2020c). Further, cognitive assessments were approved particularly in the young stroke-survivor with cognitive problems and when risk assessment for dementia was incorporated into clinical care at the six-month review (Tang et al., 2020c). Unfortunately, in the UK, the percentage of stroke-survivors receiving six-month reviews is still suboptimal with only 32% of eligible patients receiving a review according to the latest annual report from SSNAP (Sentinel Stroke National Audit Programme, 2020). Even if patients are able to be reviewed at 6 months, the requirements from SSNAP simply ask whether the patient was screened for mood, behaviour or cognition since discharge using a validated tool and whether support was offered (https://www.strokeaudit.org/SupportFiles/Documents/Clinical-Datasets-and-Help-Notes/SSNAP-Core-Dataset-4-0-0.aspx). Although there is no recommended cognitive screen for stroke patients dictated by SSNAP or national guidance, there is

a requirement to assess how many patients have received screening. However, the reporting of SSNAP groups mood, behaviour and cognition together as a single category so it is not entirely clear what proportion of patients have had a cognitive or mood screen or indeed both. In the latest available SSNAP periodic report (July to September 2019), just over a third (36%) of stroke-survivors who were eligible managed to receive a six-month review and around 1 in 4 required additional support (Sentinel Stroke National Audit Programme, 2019b). Of these, around 1 in 5 patients did not receive a screen for mood, behaviour or cognition (Sentinel Stroke National Audit Programme, 2019b). Although the total number screened are an improvement from previous annual figures, as around than 1 in 4 stroke-survivors did not get screened for mood, behaviour or cognition in the 2013–2014 annual report, the proportion of stroke-survivors not receiving a screen has remained stagnant since 2016-2017 (Sentinel Stroke National Audit Programme, 2019a). However, the case for cognitive screening at the 6-month review was felt to be important in those who were younger and also when risk dementia assessment tools were involved (Tang et al., 2020c). To achieve routine cognitive assessment it may well be that several changes could be suggested to the six-month review: a) for cognition screening to be made into a separate category on SSNAP reporting; b) a risk assessment tool to be considered in order to prompt clinicians to conduct a cognitive screen; and, c) a universally accepted stroke-specific cognitive screen to be agreed upon for example the OCS. There also needs to be some uniformity not just in terms of the screening tools used, but also how cognitive assessment is incorporated into these clinical reviews, so the clinician knows how to conduct and respond to them. This is because according to the latest periodic SSNAP report, there is a great variety in the professional backgrounds of individuals conducting the reviews (Sentinel Stroke National Audit Programme, 2019b) for example, secondary care clinicians (8.2%); stroke coordinators (33%); therapists (13.4%); district/community nurses (9.8%) and voluntary service employees (11.5%) (Sentinel Stroke National Audit Programme, 2019b). Importantly, almost 1 in 5 (19.5%) of these reviews are conducted by telephone, with some even being conducted via post (0.3%) or online (0.1%) (Sentinel Stroke National Audit Programme, 2019b); similar approaches would make cognitive testing particularly challenging.

8.4 Clinical Implications

Findings from my research (Tang et al., 2017a) support recommendations from experts in clinical guidance (Intercollegiate Stroke Working Party, 2016) and

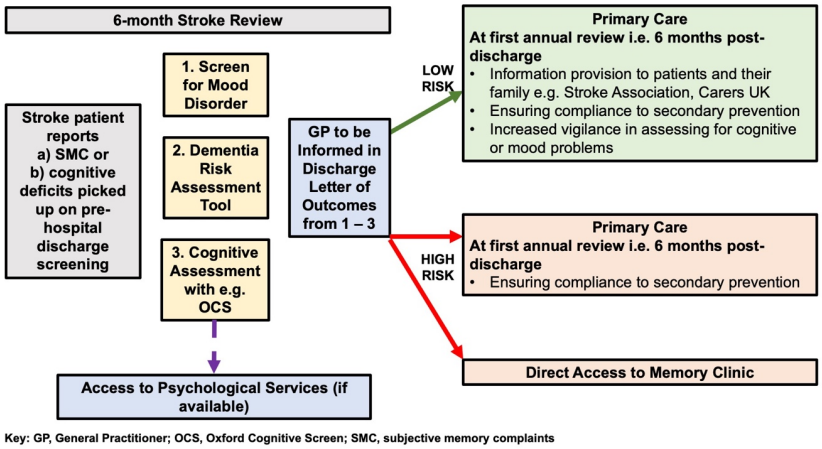
findings from qualitative studies, which were synthesised (Pindus et al., 2018). There are consistent reports that improvements in care can be achieved through collaborations between primary care teams with hospital/specialist care, particularly in terms of follow-up and annual review (Intercollegiate Stroke Working Party, 2016). The Intercollegiate Stroke Working Party recommends that:

"*People with stroke, including those living in a care home, should be offered a structured health and social care review at six months and 1 year after the stroke, and then annually. The review should consider whether further interventions are needed, and the person should be referred for further specialist assessment if a) new problems are present; b) the person's physical or psychological condition, or social environment has changed."* (Intercollegiate Stroke Working Party, 2016).

The aim of these reviews is to identify any ongoing needs that require additional intervention and referral for specialist assessment (Intercollegiate Stroke Working Party, 2016).

After the 6-month review, patients are invited to an annual review by their GP. As part of the Quality and Outcomes Framework, GPs are required to keep a register of stroke or TIA patients. They are also required to reduce the occurrence of recurrent stroke by addressing vascular risk factors, for example ensuring good blood pressure control, prescribing and compliance of antiplatelet or anti-coagulant medication as appropriate and offering support to stop smoking (NHS Digital, 2019). There is no requirement (or incentive) for GPs to address cognitive assessment post-stroke since the dementia enhanced service was removed (National Health Service (England), 2015). This service had previously incentivised GPs to undertake case finding for those at-risk of dementia which included patients aged 60 or over who had a previous stroke (National Health Service (England), 2015). From the findings of this PhD, a revised pathway (figure 1) could be a way to address this gap.

Figure 1. Proposed Integrated Pathway



Key: GP, General Practitioner; OCS, Oxford Cognitive Screen; SMC, subjective memory complaints

In secondary care, it is important that services recognise the importance of picking up cognitive concerns in a timely fashion. The potential to develop dementia following a stroke is not a new finding and despite this, assessments to identify and intervene in cognitive deficits remains under resourced and under developed as evidenced by for example the limited amount of psychological services available when compared to physical rehabilitation (Care Quality Commission, 2011). It may be increasingly difficult to increase psychological resources so that there is uniformity in care, which means stroke patients require other objective assessments so we can risk-stratify and stream individuals to the appropriate services. The following changes could be implemented to facilitate this:

8.4.1 Recommendations for Clinical Practice (1): SSNAP Dataset

Paper 1 of this thesis adds to the literature in terms of the frequency and burden of cognitive difficulties experienced by stroke-survivors (Tang et al., 2018a). In order to fully comprehend the burden of cognitive problems post-stroke when auditing, one recommendation would to be to ensure that the SSNAP dataset has a separate section for cognition i.e. question 8.2 “was the patient screened for behaviour or cognition using a validated tool” could be changed so that cognition is an independent outcome. Although mood and cognitive problems can co-exist, mood issues such as anxiety or depression tend to be more obvious to the clinician

conducting an assessment than subtle cognitive difficulties. In 2018, the Stroke Association undertook a large survey on the lived experience of strokes. In their report, although around three quarters of stroke survivors experience at least one mental health problem (e.g. anxiety, depression or even suicidal thoughts); however, 9 out of 10 stroke survivors experience at least one cognitive effect with memory problems affecting 83% of stroke patients, which is higher than the highest physical impact (i.e. on balance at 82%) (Stroke Association, 2018b). It is clear from the survey by the Stroke Association that there is a significant burden of both cognitive and mood problems and this needs to be picked up separately so appropriate services can be tailored to the individual needs of the patient.

8.4.2 Recommendations for Clinical Practice (2): Patient-Led Post-Stroke Reviews

There is consistent evidence and argument for patient led reviews so that they are targeted to meet patient needs (Abrahamson and Wilson, 2019b, McKevitt et al., 2011) which may be different to clinician priorities. Paper 2 in this PhD has highlighted the impact on patients (Tang et al., 2020a), which may not be so obvious to healthcare professionals because patients have managed to adapt. McKevitt and colleagues also specifically commented on the need to develop primary care-based strategies to assess and meet the long term unmet needs encountered by patients (McKevitt et al., 2011). Andrew and colleagues echoed this recommendation and also highlighted support for caregivers in the community (Andrew et al., 2015). To further support families affected by stroke, there needs to partnerships between them and service providers via a network which includes health and social care as well as voluntary organisations (Perry and Middleton, 2011). Long term stroke care should be consistent, targeted and more bespoke to address ongoing or new needs but also enable gaps in care to be highlighted (Forster et al., 2015). This will require regular and multiple reviews so there needs to be a connection and pathway from specialist services into primary care.

8.4.3 Recommendations for Clinical Practice (3): Proposed Changes to the Six-month Review

Papers 2 – 4 have highlighted current gaps and challenges throughout the care pathway (Tang et al., 2017a, Tang et al., 2018c, Tang et al., 2020a). Even healthcare professionals themselves have admitted to making assumptions in who manages what aspect of care (Tang et al., 2017a) highlighting a lack of clearly

defined roles and responsibilities in a clinical pathway, which may hinder integrated working. There needs to be a clear direction of care to ensure those at-risk of dementia are not missed.

As highlighted by the Delphi study in paper 7 (Tang et al., 2020c), there are certain assessments that could be included at the six-month review which could help streamline those into the appropriate levels of intervention and care. One further recommendation is the need for uniformity in the screening assessments performed for both mood and cognition. Although there are those that are still not receiving any form of cognitive screen at a time when it is most appropriate, the SSNAP audit reports that 93% of patients receive mood and cognition screening within 6 weeks of admission, although only 5% of stroke patients in hospital are found to be applicable for psychology review (Sentinel Stroke National Audit Programme, 2020). One approach would be for patients who display some cognitive deficit on the initial screen to be highlighted at the six-month review for further, more formal and detailed cognitive assessment. Paper 5 has highlighted that current risk prediction models do not work well in stroke populations, which means stroke-specific models need to be developed before implementing them in clinical practice (Tang et al., 2020b). Further in paper 6, again there needs to be care in whom we offer this assessment to as there may be concerns about how it will affect their recovery as well as the underlying fear of a potential dementia diagnosis (Tang et al., 2019). But if patients would like to undergo this assessment, then as paper 7 highlights, there are benefits to this approach (Tang et al., 2020c):

Firstly, there is seemingly a connection between carrying out the risk assessment and then also clinicians feeling it is important to carry out a cognitive assessment. An example of such a cognitive screen would be the OCS which has been adapted across different international populations (Garcia-Manzanares et al., 2020, Huygelier et al., 2019, Robotham et al., 2020, Shendyapina et al., 2019, Valera-Gran et al., 2019) and has been found to be more sensitive than the MMSE in detecting cognitive impairment in stroke patients (Mancuso et al., 2018). It also detects cognitive deficits not picked up by another common dementia cognitive screening tool, the MoCA (Demeyere et al., 2016). This will then enable a baseline assessment to be carried out and if local psychological services are available they could also be referred for targeted interventions. Further it has been shown that cognitive impairment (no dementia) at 3 months post-stroke is a significant predictor

of long term incidence of dementia in stroke patients (Allan et al., 2011). This highlights that there needs to be some sort of mechanism or pathway for clinicians to risk assess those who have some cognitive impairment shortly after their stroke so that a dementia diagnosis is not missed.

The second benefit of a dementia risk assessment tool is the ability to stratify the management of patients with new memory/cognitive deficits. In paper 7, participants felt that if they were found to be high risk then they should be referred to the memory clinic (Tang et al., 2020c). This would enable them to be assessed for a diagnosis of post-stroke dementia and then provided with the necessary intervention and support. This is particularly important as the incidence of dementia is nearly 50 times higher in the year after a major stroke compared to the general population (Pendlebury and Rothwell, 2019). Meaning that if they were found to be at high risk of dementia with a validated tool at the 6-month review, then they could be referred on in a timely fashion without delay. This could be done directly from stroke services so that at-risk patients are not missed upon discharge.

8.4.4. Recommendations for Clinical Practice (4) Better Integration of Primary and Secondary Care Services

To ensure the flow of care continues and does not stop abruptly following specialist service discharge, specialist pathways need to be better integrated across the primary-secondary care interface. Patients and their families have already expressed concerns and barriers to seeking help in primary care in paper 4 (Tang et al., 2018c). Stronger links between primary and secondary care were also identified as a facilitator to improved care in this field by clinicians in paper 3 (Tang et al., 2017a). This could be facilitated through standardised communication with the GP, for example by providing them with detailed information of the assessments carried out in stroke services especially regarding cognition. As highlighted by participants in the Delphi study, the key for both high and low risk groups then needs to be ensuring secondary prevention is adequate to prevent recurrent stroke which increases an individual's risk of future dementia (Pendlebury and Rothwell, 2009). The difference between the two groups would be where they would be referred to in the clinical pathway depending on the level of risk.

It is then important that those deemed to be at lower risk are not neglected. By virtue of their stroke, they are at higher risk than the general population to develop dementia anyway (Kuzma et al., 2018). This means that primary care clinicians need

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to have access to information and resources which would aid them to assist stroke patients and their families to identify any day-to-day deficits which might indicate the need for memory clinic referral in the future. This can be reviewed regularly at their annual reviews and should be in addition to the current measures carried out which at present simply addresses secondary prevention.

8.5 Implications for Research

8.5.1 Dementia Risk Prediction Models for Stroke Populations

There is an ever-increasing number of risk prediction models for dementia (Tang et al., 2015, Hou et al., 2019) and yet none are currently in clinical use. There clearly needs to be a balance between accuracy of the models as well as the number, complexity and cost of the variables needed to obtain an accurate risk assessment (Warren-Gash, 2019). Dementia risk models have traditionally used regression modelling but there is a growing body of work that uses machine learning algorithms to develop dementia risk models (Goerdten et al., 2019). Machine learning uses computational methods in order to find complex patterns in data which are then used to make clinical predictions. They could for example be used to identify variables to be used in a dementia risk model or be used to distinguish normal cognition versus dementia on brain imaging. However, machine learning methods to predict dementia risk from neuroimaging are not yet ready to be used because it does not reliably differentiate between clinically relevant disease categories (Pellegrini et al., 2018). The models tend to do well in differentiating healthy controls from Alzheimer's Disease but less well when mild cognitive impairment categories are involved and when it has to differentiate between mild cognitive impairment and AD (Pellegrini et al., 2018). Given the frequency of cognitive impairment in stroke, this is a significant barrier to the implementation of such models into clinical practice. There also tends to be an overreliance on one data source and this can limit generalisability (Goerdten et al., 2019). It may well be that the focus of future stroke-specific dementia models looks to incorporate known predictors which are universally available across specialist settings such as neuroimaging markers as discussed above. This will require more interdisciplinary working, collaborations across cohorts and clearer and standardised definitions of variables to be effective. Ideally, these models will still contain some modifiable risk variables so that an individual can potentially reduce their risk. These modifiable risk factors could be targeted by intervention trials to, more likely, delay the onset of cognitive decline and dementia, or improve quality of life rather than reduce the frequency of dementia.

8.5.2 Development of Primary Care Roles in Stroke

To date, stroke care has mainly been found in hospital settings with primary care responsible for longer term secondary prevention. However, this ignores the fact that primary care could play a greater role in ensuring that patients receive better cognitive support and assessment. But this requires standardised communication from stroke services as well as the provision of resources to enable the GP to support the stroke patient and their family. Given the lack of emphasis placed on cognitive care post-stroke, the first step would be to assess whether GPs and the clinical team in the community such as practice and district nurses, who may be the ones carrying out chronic care reviews, are aware of the link between stroke and dementia and the risk involved. There may be a professional knowledge gap which needs to be addressed before such services can be offered to support these patients. Further, if stroke-specific cognitive screening tools such as the OCS are to be used in primary care teams to detect those who may be at risk of an underlying dementia diagnosis in the long-term then again it needs to be assessed how feasible and acceptable such a screen would be and how it compares to shorter cognitive screens that GPs are more familiar with.

8.5.3 Multimodal Interventions to Reduce Future Risk of Dementia in Stroke

One criticism of risk assessing individuals for dementia, particularly post-stroke as some of our participants said in our qualitative study, is the lack of interventions following assessment (Tang et al., 2019). Previous trials have been mixed when it comes to intensive intervention and subsequent cognitive outcome. Some examples include the “Prevention of Decline in Cognition after Stroke Trial” (n=83), which found that intensive BP and lipid lowering did not alter cognition following recent stroke (Bath et al., 2017). Similarly, intensive BP treatment alone in first-ever stroke patients did not result in reduction in MCI or dementia diagnoses after 1 year (Ihle-Hansen et al., 2015). When patients (n=195) were allocated to either vascular risk factor intervention (information provision, optimised medical treatment to treat risk factors such as BP, cholesterol, homocysteine and BMI to target, tailored advice regarding risk factor management and treatment plan sent to the GP) or usual care, again, there was no demonstrable effect on cognition at 12-months follow-up (Ihle-Hansen et al., 2014). The Austrian Polyintervention Study to Prevent Cognitive Decline after Ischaemic Stroke (n=101 randomised into intervention) assessed whether an intensive multimodal intervention (adequate BP, lipid and glycaemic control, healthy diet, exercise and cognitive training) over a

longer period of 24 months could prevent cognitive decline after stroke (Matz et al., 2015). Again, this sample did not demonstrate any significant benefit despite a longer follow-up duration (Matz et al., 2015). In an earlier trial (the Perindopril Protection Against Recurrent Stroke Study), with a larger sample (n=6105) and longer mean follow-up time of 3.9 years, active treatment of blood pressure did reduce the risk of cognitive decline but this was more pronounced when associated with recurrent stroke (Tzourio et al., 2003). There are ongoing trials such as the AFIVASC ("physical activity in vascular cognitive impairment") group who are looking at whether physical activity alone can affect cognitive status in patients with vascular cognitive impairment or who have had previous stroke or TIA (Verdelho et al., 2019). Results from another trial looking at vascular risk factor management (BP, lipids, blood glucose and atrial fibrillation) and cognitive outcome are awaited (Myint et al., 2017). With regards to intervention, pharmacological treatment is also being trialled. Following the findings of the LACunar Intervention-1 trial (Blair et al., 2019), the results of the LACunar intervention-2 trial are currently awaited (Wardlaw et al., 2020). Here, the study team are assessing the efficacy of cilostazol versus isosorbide mononitrate or both with cognition as a secondary outcome in the hope of proceeding to a phase 3 trial (Wardlaw et al., 2020).

The lack of positive findings on cognition in stroke could be due to risk stratification as well as smaller sample sizes and duration of intervention. The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability is a well-known randomised controlled trial which did find that a multidomain intervention consisting of diet, exercise, cognitive training and vascular risk monitoring could improve or maintain cognitive functioning (Ngandu et al., 2015). Here the sample size was larger (n=2654), the follow-up duration was 2 years and importantly they used the raised CAIDE score as an inclusion criteria with the mean dementia risk score of 8.3 in those enrolled into the trial (Ngandu et al., 2014). A similar approach could be used in stroke trials once a stroke specific dementia risk score is established.

8.6 Conclusion

The incidence of post-stroke dementia will only increase due to longer survival following a stroke and successful primary (and secondary) prevention. Increasing numbers of people living with dementia will lead to significant health, social and societal costs. Stroke care has traditionally focussed heavily on acute care and physical rehabilitation but there is consistent evidence for further resources and

research into the assessment and management of the cognitive aspects also particularly if we are to reduce the risk of future post-stroke dementia cases. This body of work has highlighted the challenges faced by stroke-survivors with cognitive/memory deficits. Yet, there is the potential for primary care and specialist stroke services to work closer together to reduce these gaps in care; gaps which may lead to missed opportunities to identify those at the greatest risk of post-stroke dementia. A clearer clinical pathway is needed that has been highlighted in this thesis from the evidence generated. There are still areas that need further work such as stroke-specific risk prediction, more personalised care and targeted interventions. It is hoped that policy makers, clinicians and other stakeholders are able to continue to highlight and make changes not only in clinical services but also across the spectrum of care in order to improve the care of stroke-survivors at risk of dementia.

Postscript

Personal reflections on the research

This PhD took the best part of six years, with many challenges presented and overcome along the way. As a clinician I have always been aware the benefit of being a clinical academic when it comes to generating research ideas, involving patients and translating my findings into clinical practice. One inherent weakness that I have always felt is that we are in danger of neglecting other aspects required to be a confident independent academic clinical researcher, namely methodological expertise. I therefore made it a priority in the six years to take up the opportunities to attend courses, educational events, speak to experts such as my supervisors regularly and then apply this learning to my own research.

I have also learnt about the balance needed as a clinical academic. During my PhD I went from being a GP trainee, to a GP partner at a practice and then changing roles to be a salaried GP. At the time, I recognised my own limitations and understood the need to find the right balance of clinical and academic work in order to make both succeed. Although I have continued to take on additional leadership roles, this has been complimentary rather than additive. Now at the end of the PhD I do believe I have found an equilibrium to enable me to realise the potential of my portfolio career as an academic GP.

An unexpected problem was the emergence of the COVID-19 pandemic. Thankfully by then the data had been collected and I was at the stage of writing up my thesis. But managing clinical work, work-life balance and also motivating myself to write proved to be challenging. I took the opportunity to immerse myself in the literature and saw the potential of what I was writing in influencing patient care which provided the final motivation required to complete this body of work.

I hope as I take the next steps in my academic career, I can continue to build on this experience I have accumulated.

Positionality Statement

Here I present my positionality with respect to my own academic training, clinical and personal experience and their relationship to the field of study.

I have always seen myself as someone who likes to question and then formulating a plan to challenge the routine. I also like visible and quantifiable results that validate my questions. This way of thinking has dictated much of my career so far. I graduated from the University of Edinburgh with a Bachelor of Science in Medical Sciences (Neurosciences), Bachelor of Medicine and Bachelor of Surgery and a Master of Science. I completed an Academic Foundation Programme and then the NIHR Academic Clinical Fellowship prior to obtaining this NIHR Doctoral Research Fellowship. I had some grounding in basic clinical research methods through participating in research projects in for example the field of dementia and risk prediction leading up to the application for PhD funding as well as obtaining a Postgraduate Diploma in Clinical Research (Ageing) at Newcastle University.

I am a pragmatist at heart as my success or failure has always been determined by the practical application of my research and how to reach the end result in a timely fashion. This has softened slightly as I've embraced the world of qualitative research and allowed the participants (rather than seeing them as data points) to speak for themselves. The opportunity to work with a variety of individuals from many backgrounds nationally and internationally was always constructive to my development, even when at the time I may have perceived some experiences negatively, although this was rare. The way I interpret both qualitative and quantitative data is very much how I see them answering the clinical research question I first posed in chapter 1. Being a pragmatist can sometimes mean I miss the richness of the data and findings presented before me as I am so focussed on how to get to the end goal. But the experience of qualitative research, experience of conducting my own research and mentoring I believe has helped soften this stance.

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Appendix A: Consent and Ethical Approval (Excluding Amendments)

NHS
Health Research Authority

London - Hampstead Research Ethics Committee
Barlow House
3rd Floor
4 Minshull Street
Manchester
M1 3DZ

Telephone: 02071048127

17 February 2016

Dr Eugene Tang
NIHR Doctoral Research Fellow
Newcastle University
Biomedical Research Building, Level 2
Campus for Ageing and Vitality
NE4 5PL

Dear Dr Tang

Study title:	**Identification and Care of Patients at Risk of Post-Stroke Dementia**
REC reference:	**16/LO/0133**
Protocol number:	**0209**
IRAS project ID:	**191417**

The Research Ethics Committee reviewed the above application at the meeting held on 10 February 2016. Thank you for attending to discuss the application alongside Dr. Christopher Price.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact the REC Manager Matt Rogerson, nrescommittee.london-hampstead@nhs.net. Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.

Ethical opinion

The members of the Committee present gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below. .

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

The Committee recognised that you had made an effort to involve patient groups in the development of the Participant Information Sheets, but would invite you to review these sheets,

with particular attention to the wording of phrases such as “As many as one in ten individuals develop dementia within a year following stroke; this rises to over a third after recurrent stroke”. The Committee also suggested increasing the font size of the typography in the Participant Information Sheet, and invite you to submit the amended sheets to the Committee should they be revised at any point.

The Committee suggested you consider offering appropriate help to participants who would experience distress or become upset during the study.

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA Approval (England)/ NHS permission for research is available in the Integrated Research Application System, at www.hra.nhs.uk or at http://www.rdforum.nhs.uk.

Where a NHS organisation’s role in the study is limited to identifying and referring potential participants to research sites (“participant identification centre”), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations.

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database. This should be before the first participant is recruited but no later than 6 weeks after recruitment of the first participant.

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from the HRA. Guidance on where to register is provided on the HRA website.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

NHS Sites

The favourable opinion applies to all NHS sites taking part in the study taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Summary of discussion at the meeting

Ethical issues raised by the Committee in private discussion, together with responses given by the researcher when invited into the meeting

The Chair telephoned you and Dr Price.

Social or scientific value; scientific design and conduct of the study

The Committee asked for a summary of the study.

You explained the evidence of increased dementia risk post stroke, and that there were problems identifying those at high risk – with people usually already at a moderate stage of dementia by the time they are assessed. You explained you wished to speak to stroke patients and professionals to find out their experience of memory problems post stroke, and identify any gaps in care.

The Committee was satisfied with this response.

Recruitment arrangements and access to health information, and fair participant selection

The Committee asked you to elaborate as to who the research team would be talking to.

You explained that you would be talking to patients, carers, stroke doctors and nurses, occupational therapists and physiotherapists.

The Committee asked a question regarding recompense for health professionals – noting that GPs and practice nurses would be recompensed but other professionals were not.

You explained that this had been suggested by the R&D manager at Newcastle PCT, with the rationale being that GPs are usually recompensed, but not secondary care teams.

The Committee suggested that any recompense measures should be done fairly and equally.

You explained that you had run a lot of research involving interviewing professionals, and that recompense was exceptional, but that advice form Newcastle PCT suggested GPs would be using their own time, whereas hospital services staff would not.

This was noted with interest by the Committee.

Favourable risk benefit ratio; anticipated benefit/risks for research participants (present and future)

The Committee asked if the research team would look at pre-morbid state regarding memory problems.

You confirmed that they would not, as there was no way for them to measure this.

The Committee suggested that this be added to the exclusion criteria.

You agreed to take this on board.

Care and protection of research participants; respect for potential and enrolled participants' welfare and dignity

The Committee asked how ill potential participants would likely be – would they be lively and thriving or debilitated, confined to wheelchairs, in an upset state of mind etc.

You explained that participants would be living at home, able to attend 6 month stroke review clinics, and only invited to take part if stroke personnel felt they were okay to do so. Every stroke patient would be routinely asked about memory problems at review, as part of national guidance, with assessment results sent to GPs. The research team would wish to improve the level of effort rather than do anything new.

The Committee noted that they recognised the importance of the study.

Following further discussion, the Committee was of the opinion that there should be suitable care available if participants were to experience distress or become upset during the study. The nature of this would be up to you and your supervisors to decide, but appropriate help might be given by the research team, or participants might be guided to an external source.

Informed consent process and the adequacy and completeness of participant information

The Committee asked if the Participant Information Sheet had been developed with the help of any patient groups.

You confirmed that a participant advisory group had helped identify some of the language used around memory problems, stroke and dementia.

The Committee suggested that some of the language used seemed a little harsh and unfriendly, and suggested that more attention could be paid to phrasing. The phrase "As many as one in ten individuals develop dementia within a year following stroke; this rises to over a third after recurrent stroke" was cited as a particular example of language which might appear harsh or unfriendly when read by someone who had recently experienced a stroke.

You agreed to review the documents.

Other ethical issues were raised and resolved in preliminary discussion before your attendance at the meeting.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Covering letter on headed paper [Cover Letter]	1.0	04 December 2015
GP/consultant information sheets or letters [GP Letter]	1.0	17 December 2015
Interview schedules or topic guides for participants [Topic Guide Patients]	1.0	01 December 2015
Interview schedules or topic guides for participants [Topic Guide Carers]	1.0	01 December 2015
Interview schedules or topic guides for participants [Topic Guide Health Professional]	1.0	01 December 2015
Letter from funder [Letter from funder (NIHR)]		21 August 2015
Letter from sponsor [Letter from sponsor]		14 December 2015

Letters of invitation to participant [Invitation Letter Patient and Carer]	2.0	09 November 2015
Letters of invitation to participant [Invitation Letter Healthcare Professional]	1.0	30 October 2015
Other [Reply following PR Sub-Committee]		29 January 2016
Participant consent form [Consent Form]	1.0	30 October 2015
Participant information sheet (PIS) [PIS Patient]	2.0	23 November 2015
Participant information sheet (PIS) [PIS Carers]	2.0	23 November 2015
Participant information sheet (PIS) [PIS Primary Care Professional]	1.0	20 November 2015
Participant information sheet (PIS) [PIS Secondary Care Professional]	1.0	20 November 2015
REC Application Form [REC_Form_23122015]		23 December 2015
Referee's report or other scientific critique report [Internal peer review]		15 December 2014
Referee's report or other scientific critique report [External peer review (NIHR)]		16 January 2015
Research protocol or project proposal [Protocol]	1.0	30 October 2015
Summary CV for Chief Investigator (CI) [CV]		04 December 2015
Summary CV for student [CV]		04 December 2015
Summary CV for supervisor (student research) [Supervisor CVs]		04 December 2015
Summary, synopsis or diagram (flowchart) of protocol in non technical language [Lay Summary]	1.0	04 December 2015

Membership of the Committee

The members of the Ethics Committee who were present at the meeting are listed on the attached sheet.

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

16/LO/0133 **Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

Signed on behalf of

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

16/LO/0133	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

Signed on behalf of
Miss Stephanie Ellis
Chair

E-mail: nrescommittee.london-hampstead@nhs.net

Enclosures: List of names and professions of members who were present at the meeting and those who submitted written comments

"After ethical review – guidance for researchers"

Copy to: Mrs Caroline Potts, Northumbria Healthcare NHS Trust Research and Development

[NHS LOGO INSERTED HERE)

Participant Identification Number: ☐ **Patient** ☐ **Carer** ☐ **Professional** ☐

Consent Form

Identification and Care of Patients at Risk of Post Stroke Dementia

Research Team: Dr. Eugene Tang, Professor Robinson, Professor Catherine Exley, Dr. Christopher Price, Dr. Blossom Stephan

	Please Initial
1. I confirm that I have read and understood the information sheet for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily	
2. I understand that participation is voluntary and can withdraw at any time without giving any reason, without my medical care or legal rights as a patient, carer or professional being affected	
3. I agree to allow the researchers to make field notes and audio recordings of the interview. I understand direct quotes may be used in the final report or scientific publications, however these will be anonymised and no personal information which could identify me will be used	
4. I understand that all data collected will be anonymised and confidential and will be stored in a locked filing cabinet and on a password protected computer located at Newcastle University.	
5. I understand that during the study if any disclosures are made that would indicate malpractice or misconduct, or suggest that any individual was in danger of harm; this information will be disclosed to the appropriate personnel.	
6. I understand that once transcribed that audio recordings of the interview will be destroyed and transcripts stored in locked files in accordance with the Data Protection Act.	
7. I agree to take part in the above research study	
8. I would like a copy of the final results	
9. I agree to my GP being informed of my participation in the study	

Name of Participant	Date	Signature
Name of Person taking consent	Date	Signature

When completed: 1 copy for participant; 1 copy for researcher file

Faculty of Medical Sciences
Newcastle University
The Medical School
Framlington Place
Newcastle upon Tyne
NE2 4HH United Kingdom

Eugene Yee Hing Tang
Institute of Health & Society (IH&S)

FACULTY OF MEDICAL SCIENCES: ETHICS COMMITTEE

Dear Eugene,

Title: External Validation of Dementia Risk Models in Stroke-Survivors
Application No: 1404/15534/2017
Start date to end date: 16/05/2017 to 01/01/2019

On behalf of the Faculty of Medical Sciences Ethics Committee, I am writing to confirm that the ethical aspects of your proposal have been considered and your study has been given ethical approval.

The approval is limited to this project: **1404/15534/2017**. If you wish for a further approval to extend this project, please submit a re-application to the FMS Ethics Committee and this will be considered.

During the course of your research project you may find it necessary to revise your protocol. Substantial changes in methodology, or changes that impact on the interface between the researcher and the participants must be considered by the FMS Ethics Committee, prior to implementation.*

At the close of your research project, please report any adverse events that have occurred and the actions that were taken to the FMS Ethics Committee.*

Best wishes,

Yours sincerely

Kimberley Sutherland
On behalf of Faculty Ethics Committee

cc.
Professor Daniel Nettle, Chair of FMS Ethics Committee
Mrs Kay Howes, Research Manager

*Please refer to the latest guidance available on the internal Newcastle web-site.

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03 May 2019

Eugene Yee Hing Tang
Institute of Health & Society

Faculty of Medical Sciences
Newcastle University
Medical School
Framlington Place
Newcastle upon Tyne
NE2 4HH

FACULTY OF MEDICAL SCIENCES: ETHICS COMMITTEE

Dear Eugene

Title: A Delphi Survey to Determine Clinical Preferences for Services Providing Care to Stroke Patients with Cognitive Impairment
Application No: 1673/10898/2018
Start date to end date: 01/04/2019 to 01/01/2020

On behalf of the Faculty of Medical Sciences Ethics Committee, I am writing to confirm that the ethical aspects of your proposal have been considered and your study has been given ethical approval.

The approval is limited to this project: **1673/10898/2018**. If you wish for a further approval to extend this project, please submit a re-application to the FMS Ethics Committee and this will be considered.

During the course of your research project you may find it necessary to revise your protocol. Substantial changes in methodology, or changes that impact on the interface between the researcher and the participants must be considered by the FMS Ethics Committee, prior to implementation.*

At the close of your research project, please report any adverse events that have occurred and the actions that were taken to the FMS Ethics Committee.*

Best wishes,

Yours sincerely

M. Holbrough

Marjorie Holbrough
On behalf of Faculty Ethics Committee

cc.
Professor Daniel Nettle, Chair of FMS Ethics Committee
Mrs Kay Howes, Research Manager

*Please refer to the latest guidance available on the internal Newcastle web-site.

Appendix B. Invitation Letters, Participant Information Sheets and Topic Guides

Invitation Letter: Health Professional

Northumbria Healthcare NHS
NHS Foundation Trust

Newcastle University

Dear colleague

Northumbria Healthcare NHS Foundation Trust is involved in a study looking to understand the care experience of stroke-survivors who have reported memory or cognitive difficulties. The study is called "**Identification and Care of Patients at Risk of Post Stroke Dementia**" and is funded by the National Institute for Health Research (NIHR).

To provide a healthcare professional's view on this area we would like to invite you to participate in one-to-one interviews with a member of the research team. You are entirely free to choose whether you wish to participate and it would not affect your employment status whatever you decide. The interview would be conducted at your place of work or Newcastle University. It should take no longer than 1 hour. If you would prefer, the interview could also be conducted by telephone. The researcher is a General Practitioner registrar employed by Newcastle University, Dr. Eugene Tang. Information you provide would not be shared or linked to your name but quotations you provide will be anonymously included in any reports or publications derived from this study.

Attached you will find an information sheet about this study which sets out in more detail why this study is being done and what it will involve. If you are interested in participating, please detach the return slip below and return it to the research team or send your details to the researcher's email address (as below and on the information sheet). A mixture of volunteers is required so you may or may not be chosen to participate however the research team will let you know either way.

Yours sincerely

Dr. Eugene Tang
NIHR Doctoral Research Fellow and Academic General Practice Registrar (ST4)
On behalf of the research team

----------Please complete and return if you wish to take part ----------

I am willing to discuss the study with the research team and happy for my contact details to be passed onto them. However I understand that I am free to withdraw at any time and with no reason. I understand a researcher will contact me to arrange a suitable time to discuss the research further.

Name: _____ Site/Ward_____

Signature: _____

Contact details (work): (email, telephone or other)

_____

Return to: Level 2, Biomedical Research Building, Campus for Ageing and Vitality, Newcastle upon Tyne NE4 5PL. Email: e.y.h.tang@newcastle.ac.uk

Northumbria Healthcare NHS
NHS Foundation Trust

Newcastle University

"**Identification and Care of Patients at Risk of Post-Stroke Dementia**"

This information describes a study to help hospitals and GPs understand what happens to people who have had a stroke, which have caused memory problems.

If you are a patient or a carer of a stroke-survivor you may wish to take part

After a stroke, a person may have problems with their memory. Occasionally the memory problems get worse and can lead to dementia. However, for many this will improve. This study will look at the care received by people who have had a stroke and described memory problems afterwards. We will look at what information they are given and the care they get from the hospital and also their GPs subsequently.

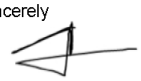
This study involves interviews with patients, their carers or family members and health professionals.

To help us understand where the gaps are and how to improve current care, we are seeking volunteers to share their experiences and views. This would involve an informal interview either in the weeks after your stroke clinic or 6 months after. Some may be interviewed at both time points. Interviews will be held at a location in hospital, Newcastle University or your home. It would take as long as you can manage but would be less than 1 hour. You are entirely free to choose whether you wish to participate or not.

The interviews are performed by Dr. Eugene Tang, a GP who is doing research at Newcastle University in collaboration with the Stroke Service at Northumbria Healthcare NHS Foundation Trust. All information received is kept confidential and individual volunteers cannot be identified. More information about the research is given in the attached leaflet. If you wish to find out more about the study before agreeing to take part please detach the return slip below and return it to the stroke team or send your details to Dr. Eugene Tang's email address, which is found on the attached sheet and below.

Thank you for considering taking part in this study. If you choose not to take part either at this stage or following contact with the team, this will not affect the care that you or your relative receives.

Yours sincerely



Dr. Eugene Tang
On behalf of the research team

----------Please complete and return if you wish to take part ----------
I am willing to discuss the project further with the research team and agree to my details to be passed onto them. However I understand that I am free to withdraw at any time and without giving a reason. I understand a researcher will contact me to arrange a suitable time to discuss the research proposal.

Name: _____ Hospital:_____

Signature: _____

Contact details: (email, telephone or other)
_____

Please hand this back to the person who gave you the information sheet or post to: Eugene Tang, Level 2, Biomedical Research Building, Campus for Ageing and Vitality, Newcastle upon Tyne NE4 5PL Email: e.y.h.tang@newcastle.ac.uk

HEALTHCARE PROFESSIONAL INVITATION LETTER

Dear colleague,

Northumbria Healthcare NHS Foundation Trust is involved in a study looking to understand the care experience of stroke-survivors who have reported memory or cognitive difficulties. The study is called "**Identification and Care of Patients at Risk of Post Stroke Dementia**" and is funded by the National Institute for Health Research (NIHR).

To provide a healthcare professional's view on this area we would like to invite you to participate in one-to-one interviews with a member of the research team. You are entirely free to choose whether you wish to participate and it would not affect your employment status whatever you decide. The interview would be conducted at your place of work or Newcastle University. It should take no longer than 1 hour. If you would prefer, the interview could also be conducted by telephone. The researcher is a General Practitioner registrar employed by Newcastle University, Dr. Eugene Tang. Information you provide would not be shared or linked to your name but quotations you provide will be anonymously included in any reports or publications derived from this study.

Attached you will find an information sheet about this study which sets out in more detail why this study is being done and what it will involve. If you are interested in participating, please detach the return slip below and return it to the research team or send your details to the researcher's email address (as below and on the information sheet). A mixture of volunteers is required so you may or may not be chosen to participate however the research team will let you know either way.

Yours sincerely

Dr. Eugene Tang
NIHR Doctoral Research Fellow and Academic General Practice Registrar (ST4)
On behalf of the research team

----------Please complete and return if you wish to take part ----------

I am willing to discuss the study with the research team and happy for my contact details to be passed onto them. However I understand that I am free to withdraw at any time and with no reason. I understand a researcher will contact me to arrange a suitable time to discuss the research further.

Name: _____ Site/Ward_____

Signature: _____

Contact details (work): (email, telephone or other)

_____

Return to: Level 2, Biomedical Research Building, Campus for Ageing and Vitality, Newcastle upon Tyne NE4 5PL. Email: e.y.h.tang@newcastle.ac.uk

Northumbria Healthcare NHS
NHS Foundation Trust

Newcastle University

Identification and Care of Patients at Risk of Post Stroke Dementia

We'd like to invite you to take part in our research study.

- *Joining the study is entirely up to you, before you decide we would like you to understand why the research is being done and what it would involve for you.*
- *Please take time to read the following information carefully and feel free to discuss it with others. We'd suggest this should take about 15 minutes.*
- *You are free to decide whether or not to take part in this study.*
- *Please ask us (contact details are available at the end of the leaflet) if there is anything that is not clear or if you would like more information*

SUMMARY

- We wish to understand the experience of stroke-survivors who subsequently develop memory and cognitive issues.
- This is important and relevant as stroke has been associated with increased risk of developing dementia in the future irrespective of whether the stroke-survivor has any other risk factors associated with dementia.
- As many as one in ten individuals will develop dementia soon after their first stroke.
- We are conducting interviews with patients, carers and health professionals in primary and secondary care
- By taking part, we will conduct interviews on issues surrounding this topic, which will last no more than an hour in a suitable location for you.
- You can stop taking part in the study at any time

WHATS INVOVLED?

Purpose and Background

As many as one in three people will experience stroke, dementia or both at some stage in their lives as stroke is currently the second most common cause of acquired cognitive impairment. Increasing survival rates associated with stroke translate to an increased number of stroke-survivors who will develop cognitive impairment. A history of stroke doubles the risk of future dementia in older stroke populations and this increase is not explained by demographic factors (such as age, sex and ethnicity), cardiovascular risk factors or by prestroke cognitive decline. As many as one in ten individuals develop dementia within a year following a stroke; this rises to over a third after recurrent stroke. There is increasing evidence that earlier diagnosis of dementia improves overall quality care by ensuring timely access to treatment, information and support. Given that this is the case, it is important to identify stroke-survivors who are at the greatest risk of developing future dementia. Our study objectives are:

1) To describe healthcare experience of stroke-survivors, who had expressed a problem with their memory following discharge from secondary care services in the community?

2) To identify what support is available from both stroke services and primary care for people who have cognitive problems from six months following a stroke?

3) To explore the facilitators and barriers in primary and secondary care to enable healthcare professionals to undertake more timely identification of individuals with cognitive deficits following a stroke, including the potential use of risk assessment tools

Through semi-structured interviews we hope to gather the views and opinions of different people involved in managing stroke-survivors with memory problems. This will include patients, carers as well as a range of health care professionals in primary and secondary care.

What would taking part involve?

If you are happy to participate in this study, please either return the slip attached to the covering invitation letter of this leaflet or email the chief investigator (Dr. Eugene Tang) with the details provided below. He will then contact you in 2- 7 days to explain what is involved in taking part, check that you are happy to take part and that you understand the research. Please feel free to ask him any questions. You will then have up to a week to decide whether you wish to participate in the study. If you are happy to continue, he will then agree a time and a location with you for your interview.

If you decide to take part you will be interviewed about the following areas:

- What support/information do stroke-survivors receive if memory, attention and concentration problems are identified?
- Your thoughts and feelings about how stroke-survivors with memory problems should be managed
- What support you would like in place for stroke-survivors with memory problems
- Your thoughts and feelings about risk assessment and early identification of those at risk of dementia

The interview will not be about deciding the exact nature of any future care but about what is currently happening and what should happen in the future.

The interview will last about 1 hour but it can be stopped at any time if you wish. The interview will be audio-recorded and participation will end once the interview has concluded. Telephone interviews are also an option.

What are the possible benefits of taking part?

Some people find it helpful to take through their experiences and feelings about the healthcare system in place. It can help us identify areas that are currently lacking particularly when identifying and helping stroke-survivors with memory problems. We hope that this research will lead to improvements in how stroke-survivors with memory and cognitive difficulties are managed. This study will feed into further studies to enable the research team to develop a clinical service framework to the benefit of these at-risk individuals.

What are the possible disadvantages of taking part?

Some people may find that talking about their experiences in managing these individuals difficult. The interview process itself can be tiring and requires up to 1 hour of your time. The interview can be paused or stopped at any point and you are free to withdraw from the study at any point.

What if something goes wrong?

If you have a concern about any aspect of this study you should speak to the researcher who will do their best to answer your questions (Dr. Eugene Tang, 0191 208 7214).

What will happen if I don't want to carry on with the study?

You are free to withdraw your consent from this study at any time for any reason and without giving a reason. Information collected may still be used but you can withdraw your consent to the use of this data if you wish.

Will my information be kept confidential?

All information collected will be kept strictly confidential and can only be accessed by members of the research team. To preserve anonymity, any information that leaves the interview location will have all

identifiable data removed and replaced by a unique study identification code. All study data will be kept at a study site in a locked filing cabinet with restricted access.

What will happen to the results of this study?

Dissemination will be via the NHS and wider care community to target patients and their families. We will also look to publish our findings in peer-reviewed journals and present them at national and international meetings. The study will also be reported to the National Institute for Health Research, who is the funding body. However you will not be identified in any of the reports or publications. A summary of the findings will be available at the end of the study.

All audio-recorded files will be stored on a secure computer network with the originals destroyed at the end of the study. Any quotations used will be anonymised in reports and publications arising from the study. Only members of the research team will listen to the recordings of the interview.

Who is organising and funding this study?

This study is funded by the National Institute for Health Research. The research team is based at the Institute of Health and Society at Newcastle University. The chief investigator for this study is Dr. Eugene Tang.

How have patients and the public been involved in this study?

Members of the public and patients have reviewed and helped design parts of this study. There is also a patient group (consisting of individuals who have had a stroke, carers of people with dementia and older members of the public with an interest in research) who has helped with the research materials used in this study. A member of the patient group also sits on the research steering group who are tasked with reviewing and providing feedback for this study.

Who has reviewed this study?

As part of the funding process, experts in the field, patients and members of the public have reviewed this study. All research in the NHS is looked at by independent panels of people called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has been granted a favourable ethical opinion by the London – Hampstead Research Ethics Committee.

Dr. Eugene Tang
Newcastle University
Level 2, Biomedical Research Building
Campus for Ageing and Vitality
NE4 5PL
Tel: 0191 208 8758
Email: e.y.h.tang@newcastle.ac.uk

Thank you for taking the time to read this information

Identification and Care of Patients at Risk of Post Stroke Dementia

We'd like to invite you to take part in our research study.

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Through semi-structured interviews we hope to gather the views and opinions of different people

involved in managing stroke-survivors with memory problems. This will include patients, carers as well as a range of health care professionals in primary and secondary care.

What would taking part involve?

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- Your thoughts and feelings about risk assessment and early identification of those at risk of dementia

The interview will not be about deciding the exact nature of any future care but about what is currently happening and what should happen in the future.

The interview will last about 1 hour but it can be stopped at any time if you wish. The interview will be audio-recorded and participation will end once the interview has concluded. Telephone interviews are also an option.

You will be compensated for your time at the standard hourly rate as advised by the North of England Commissioning Support's research and development team.

What are the possible benefits of taking part?

Some people find it helpful to take through their experiences and feelings about the healthcare system in place. It can help us identify areas that are currently lacking particularly when identifying and helping stroke-survivors with memory problems. We hope that this research will lead to improvements in how stroke-survivors with memory and cognitive difficulties are managed. This study will feed into further studies to enable the research team to develop a clinical service framework to the benefit of these at-risk individuals.

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Some people may find that talking about their experiences in managing these individuals difficult. The interview process itself can be tiring and requires up to 1 hour of your time. The interview can be paused or stopped at any point and you are free to withdraw from the study at any point.

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What will happen if I don't want to carry on with the study?

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Will my information be kept confidential?

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How have patients and the public been involved in this study?

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Who has reviewed this study?

As part of the funding process, experts in the field, patients and members of the public have reviewed this study. All research in the NHS is looked at by independent panels of people called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has been granted a favourable ethical opinion by the London – Hampstead Research Ethics Committee.

Further information and contact details

For further information about the study please contact the chief investigator, Dr. Eugene Tang

Dr. Eugene Tang
Newcastle University
Level 2, Biomedical Research Building
Campus for Ageing and Vitality
NE4 5PL
Tel: 0191 208 8758
Email: e.y.h.tang@newcastle.ac.uk

Thank you for taking the time to read this information

What will happen to the results of this study?

We plan to share the findings with patient groups, GPs, consultants and other professionals who care for people after their stroke. We will also look to publish our findings in journals and present them at national and international meetings. The study will also be reported to the National Institute for Health Research, who is funding this study. However you will not be identified in any of the reports or publications. A summary of the findings will be available at the end of the study. We can send you a copy if you are interested.

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Newcastle University, Level 2,
Biomedical Research Building, Campus for Ageing and Vitality, NE4 5PL
Tel: 0191 208 8758
Email: e.y.h.tang@newcastle.ac.uk

Further information

You can get general advice about stroke and memory problems after stroke from:
Stroke Association (North East)
Hawthorn House, Heaton Road, Byker,
Tyne and Wear, NE6 1SD
Tel: 0191 2760595
Weekly meetings on Monday

Thank you for taking the time to read this information

Northumbria Healthcare NHS Foundation Trust

Newcastle University

INFORMATION ABOUT THE RESEARCH: PATIENT INTERVIEW

Identification and Care of Patients at Risk of Post-Stroke Dementia

We'd like to invite you to take part in our research study.

- *Joining the study is entirely up to you. Before you decide we would like you to understand why the research is being done and what it would involve for you.*
- *Please take time to read the following information carefully and feel free to discuss it with friends and relatives if you wish.*
- *You are free to decide whether or not to take part in this study. If you choose not to take part, this will not affect the care you get from your own doctors.*
- *Please ask us (contact details are available at the end of the leaflet) if there is anything that is not clear or if you would like more information*

SUMMARY

- We wish to understand the experience of stroke-survivors who may go on to develop memory problems shortly after their stroke.
- For the majority of people who have had a stroke, their memory improves. For some their memory problems can worsen and a few can develop dementia.
- At present we do not know how to separate these two sets of patients nor do we know what care they receive to support them if they do develop memory problems.
- We are conducting interviews with patients, carers and health professionals (hospital and in General Practice).
- By taking part, we will conduct interviews on issues surrounding this topic, which will last no more than an hour in a suitable location for you.
- You can decide not to take part in the interview at any time

Purpose and Background

This study aims to understand the care experience of people who have had a stroke and develop memory problems. We will interview patients, carers and the healthcare professionals looking after them. A small proportion of people who have had a stroke are at further risk of developing dementia in the future. However it is unclear how we identify these individuals who are at higher risk. This is important as earlier diagnosis of dementia can lead to improved support, information provision and access to treatments. To achieve this we must first understand what is the current level and standard of care for people with memory problems after stroke so that we can identify what gaps in care there might be. To help us do this, we wish to gather your views and opinions as someone who has had a stroke and have expressed that you also have memory problems after your stroke.

What would taking part involve?

If you are happy to participate in this study, please either return the slip attached to the letter of this leaflet or email the researcher (Dr. Eugene Tang). He will contact you within a week to explain what is involved and check that you are happy to take part. Please feel free to ask him any questions. You will then have a week to decide whether you wish to participate in the study. If you are happy to continue, he will then agree a time and a location with you for an interview. You will be interviewed in one of three groups:

1) In the coming weeks after your stroke clinic appointment
2) 6 months following your stroke clinic appointment
3) In the coming weeks after your clinic review AND 6 months later

He will talk to you about:

- The support/information you received after your stroke clinic review
- Your thoughts and feelings about memory problems developing following a stroke
- Your ideas for improving care for people who have had a stroke and develop memory problems
- Your thoughts and feelings about assessing risk and early identification of those at risk of dementia if you have had a stroke

The interview will not be about deciding the exact nature of any future care but about what is currently happening and what should happen in the future. It is not a memory test. The interview will last about 1 hour but it can be stopped at any time if you wish. The interview will be audio-recorded and participation will end once the interviews have concluded. This study should not incur any extra expense to you but if travel expenses are incurred for example by travelling to the interview site this will be reimbursed.

What are the possible benefits of taking part?

Some people find it helpful to talk through their experiences and feelings about the healthcare system in place. It can help identify areas that are currently lacking particularly when helping stroke-survivors with memory problems. Taking part in the interview may also increase your awareness of the options and support available.

What are the possible disadvantages of taking part?

Some people may find that talking about their experiences difficult and distressing. The interview process itself can be tiring. The interview can be paused or stopped at any point and you are free to withdraw from the study at any point without affecting your current care.

What if something goes wrong?

If you have a concern about any aspect of this study you should speak to the researcher who will do his best to answer your questions (Dr. Eugene Tang, 0191 208 8758). If you remain unhappy and wish to complain formally, you can do this via the NHS Complaints Procedure. Details can be obtained from your GP.

What will happen if I don't want to carry on with the study?

You are free to withdraw your consent from this study at any time for any reason and without giving a reason. Information collected may still be used but you can withdraw your consent to the use of this data if you wish.

Will my information be kept confidential?

All information collected will be kept strictly confidential and can only be accessed by members of the research team. To preserve anonymity, any information that leaves the interview location will have all identifiable data removed and replaced by a unique code. All study data will be kept at a study site in a locked filing cabinet with restricted access.

What will happen to the results of this study?

We plan to share the findings with patient groups, GPs, consultants and other professionals who care for people after their stroke. We will also look to publish our findings in journals and present them at national and international meetings. The study will also be reported to the National Institute for Health Research, who is funding this study. However you will not be identified in any of the reports or publications. A summary of the findings will be available at the end of the study. We can send you a copy if you are interested.

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Northumbria Healthcare NHS
NHS Foundation Trust

Newcastle University

INFORMATION ABOUT THE RESEARCH: CARER INTERVIEW

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SUMMARY

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The interview will not be about deciding the exact nature of any future care but about what is currently happening and what should happen in the future. It is not a memory test. The interview will last about 1 hour but it can be stopped at any time if you wish. The interview will be audio-recorded and participation will end once the interviews have concluded. This study should not incur any extra expense to you but if travel expenses are incurred for example by travelling to the interview site this will be reimbursed.

What are the possible benefits of taking part?

Some people find it helpful to talk through their experiences and feelings about the healthcare system in place. It can help identify areas that are currently lacking particularly when helping stroke-survivors with memory problems. Taking part in the interview may also increase your awareness of the options and support available as a carer.

What are the possible disadvantages of taking part?

Some people may find that talking about their experiences difficult and distressing. The interview process itself can be tiring. The interview can be paused or stopped at any point and you are free to withdraw from the study at any point without affecting your or your care receiver's current care.

What if something goes wrong?

If you have a concern about any aspect of this study you should speak to the researcher who will do his best to answer your questions (Dr. Eugene Tang, 0191 208 8758). If you remain unhappy and wish to complain formally, you can do this via the NHS Complaints Procedure. Details can be obtained from your GP.

What will happen if I don't want to carry on with the study?

You are free to withdraw your consent from this study at any time for any reason and without giving a reason. Information collected may still be used but you can withdraw your consent to the use of this data if you wish.

Will my information be kept confidential?

All information collected will be kept strictly confidential and can only be accessed by members of the research team. To preserve anonymity, any information that leaves the interview location will have all identifiable data removed and replaced by a unique code. All study data will be kept at a study site in a locked filing cabinet with restricted access.

IDENTIFICATION AND CARE OF PATIENTS AT RISK OF POST STROKE DEMENTIA

INTERVIEW TOPIC GUIDE

N.B. There are not meant to be prescriptive but offer a guide for these interviews. The interviews are deliberately flexible in nature to allow participants to raise or explore issues, which are important to them

Introduction and housekeeping

- Researcher to introduce an overview and the aim of the study. Need to reiterate participant's right to withdraw, pause the interview and confidentiality issues
- Seek permission to audio-record interview
- Ask whether they have any further questions
- Receive informed consent

Current Care Experience

- What is your experience of stroke-survivors who develop memory or cognitive difficulties when you review them after their stroke?
- What advice or support do you provide to stroke-survivors when they do experience memory or cognitive difficulties?
- What factors influence how easy or difficult it is to provide the advice and support required by these individuals?
- What are your opinions as to the amount or level of support available for stroke-survivors with memory or cognitive difficulties?
- Are you aware of any risk assessment that currently takes place in clinical practice for dementia either in primary or secondary care? What is your experience and opinion of these assessments?

Views on Future Care

- What do you think might be the benefits in identifying stroke-survivors at risk of dementia earlier? Specifically:
    - For the patient
    - For their families
    - For doctors, nurses and the healthcare system
    - If not beneficial why not?
- Do you have any views on how we could identify those at risk of dementia?
- What do you think might be the benefits to better integration and involvement of the GP when memory difficulties do appear? Please elaborate - How could this be achieved?
- Can you think of any drawbacks or barriers when trying to improve the integration and communication between primary and secondary care services?

Views on Risk Assessment

- (Provide example of a risk assessment tool in dementia): What are your views in a risk assessment tool such as this to help identify stroke-survivors who are most at risk of dementia in the future?
- Where could such an assessment take place?
- What are the benefits or problems associated with:
    - The delivery of the tool itself (by whom? where?)
    - The variables used in the tool
    - The outcome of the tool (high vs. low risk)

IDENTIFICATION AND CARE OF PATIENTS AT RISK OF POST STROKE DEMENTIA

INTERVIEW TOPIC GUIDE (IMMEDIATELY AFTER 6 MONTH DISCHARGE FROM STROKE-CLINIC)

N.B. There are not meant to be prescriptive but offer a guide for these interviews. The interviews are deliberately flexible in nature to allow participants to raise or explore issues, which are important to them

Introduction and housekeeping

- Researcher to introduce an overview and the aim of the study. Need to reiterate participants right to withdraw, pause the interview and confidentiality issues
- Seek permission to audio-record interview
- Ask whether they have any further questions
- Receive informed consent

Current Care Experience

- What is your experience of the care you've received since your stroke?
- Could you describe any situations before you stroke where you encountered memory problems?
- What is your experience/your relative/care receiver's experience of the stroke service at 6 months with regards to your memory difficulties? Specifically
    - What questions were asked about your memory difficulties?
    - What was explained to you about your memory difficulties?
    - What support or advice was given to you regarding the new memory difficulties you've described?
- What are your opinions on the advice and support given by the team with regards to these new difficulties? What are your families' opinion on the support and advice you've received?
- What or where would you seek for support or information if your memory deteriorates further or does not improve?
- Describe risk assessment (Risk assessment is where health professionals use a number of factors that are unique to you in combination to guide deem whether you are high or low risk of a problem such as dementia. This enables them to tailor their advice, support and management to each individual). What is your experience of risk assessment of dementia if any?

Views on Future Care

- What do you think might be the benefits in identifying stroke-survivors at risk of dementia earlier? Specifically:
    - For the patient
    - For their families
    - For doctors, nurses and the healthcare system
    - If not beneficial why not?
- Do you have any views on how healthcare professionals could identify those at risk of dementia?
- What do you think might be the benefits or barriers when involving the GP when memory difficulties do appear? Please elaborate - How could this be achieved?
- Can you think of any drawbacks in hospitals and GPs working together to manage this problem?

Views on Risk Assessment

- (Provide example of a risk assessment tool in dementia): What are your views in a risk assessment tool such as this to help identify stroke-survivors who are most at risk of dementia in the future?
- What are the benefits or problems associated with:
    - The delivery of the tool itself (by whom? where?)
    - The variables used in the tool
    - The outcome of the tool (high vs. low risk)

TOPIC GUIDE (1 YEAR POST-STROKE FIRST INTERVIEW)

Introduction and housekeeping

- Researcher to introduce an overview and the aim of the study. Need to reiterate their right to withdraw, pause the interview and confidentiality issues
- Seek permission to audio-record interview
- Ask whether they have any further questions
- Receive informed consent

Current Care Experience

- What is your experience of the care you've received since your stroke?
- Can you tell me how your memory has been? If you have had problems can you give me any examples e.g. have you remembered to take your medications?
- Have you needed to seek help for your memory difficulties at any point in the last 6 months? If yes, please elaborate
- Have you approached any health professional with your memory difficulties?
    - If yes – Who did you see? Why did you approach them? What are your opinions into the support/advice/management you were offered
    - If no – are there any reasons why you did not (any barriers to accessing healthcare services)?
- Has your memory affected your day to day living in the past 6 months
    - If so, how has it affected your day-to-day living and how have you managed this?
    - If not, are there any reasons why this has been the case?
- Risk assessment is where health professionals use a number of factors that are unique to you in combination to guide deem whether you are high or low risk of a problem such as dementia. This enables them to tailor their advice, support and management to each individual. Are you aware or have you been subject to any risk assessment that currently takes place for dementia? If yes – have you seen any benefits or problems with this approach?

Views on Future Care

- What do you think might be the benefits in identifying stroke-survivors at risk of dementia earlier? Specifically:
    - For the patient
    - For their families
    - For doctors, nurses and the healthcare system
    - If not beneficial why not?
- Do you have any views on how healthcare professionals could identify those at risk of dementia?
- What do you think might be the benefits or barriers when involving the GP when memory difficulties do appear? Please elaborate - How could this be achieved?
- Can you think of any drawbacks in hospitals and GPs working together to manage this problem?
- Having lived with memory difficulties following your stroke:
    - Are there in gaps in support/care that you feel are present which might be a barrier to better care?
    - Have you got any opinions on what could be put in place to better support you in the community?

Views on Risk Assessment

- Provide example of a risk assessment tool in dementia): What are your views in a risk assessment tool such as this to help identify stroke-survivors who are most at risk of dementia in the future?
- What are the benefits or problems associated with:
    - The delivery of the tool itself (by whom? where?)
    - The variables used in the tool
    - The outcome of the tool (high vs. low risk)

TOPIC GUIDE (1 YEAR POST-STROKE SECOND INTERVIEW)

Introduction and housekeeping

- Researcher to introduce an overview and the aim of the study. Need to reiterate their right to withdraw, pause the interview and confidentiality issues
- Seek permission to audio-record interview
- Ask whether they have any further questions
- Receive informed consent

Current Care Experience

- What is your experience of the care you've received since your stroke?
- Can you tell me how your memory has been? If you have had problems can you give me any examples e.g. have you remembered to take your medications?
- Have you needed to seek help for your memory difficulties at any point in the last 6 months?
- Have you approached any health professional with your memory difficulties?
    - If yes – Who did you see? Why did you approach them? What are your opinions into the support/advice/management you were offered
    - If no – are there any reasons why you did not (any barriers to accessing healthcare services)?
- Has your memory affected your day to day living in the past 6 months
    - If so, how has it affected your day-to-day living and how have you managed this?
    - If not, are there any reasons why this has been the case?
- We talked about risk assessment at our last interview. Since we have met have you been made aware or have you been subject to any risk assessment that currently takes place for dementia? If yes – have you seen any benefits or problems with this approach?

Views on Future Care

- Having lived with memory difficulties following your stroke:
    - Are there in gaps in support/care that you feel are present which might be a barrier to better care?
    - Have you got any opinions on what could be put in place to better support you in the community?
- Has your opinion changed as to whether you think we should be identifying stroke-survivors at risk of dementia earlier? Please elaborate

Views on Risk Assessment

- (Provide example of risk assessment tool in dementia): Last time we met we talked about whether a risk assessment tool would be clinically useful? What do you think about this now? Please elaborate

IDENTIFICATION AND CARE OF PATIENTS AT RISK OF POST STROKE DEMENTIA

INTERVIEW TOPIC GUIDE (AT 6 MONTH DISCHARGE FROM STROKE-CLINIC)

N.B. There are not meant to be prescriptive but offer a guide for these interviews. The interviews are deliberately flexible in nature to allow participants to raise or explore issues, which are important to them

Introduction and housekeeping

- Researcher to introduce an overview and the aim of the study. Need to reiterate participant's right to withdraw, pause the interview and confidentiality issues
- Seek permission to audio-record interview
- Ask whether they have any further questions
- Receive informed consent

Current Care Experience

- What is your experience of the care received since your family member/care receiver's stroke?
- What is your experience as a care provider of the stroke service at 6 months with regards to their memory difficulties? Specifically
    - What questions were asked about their memory difficulties?
    - What was explained to you about their memory difficulties?
    - What support or advice was given regarding the new memory difficulties they've described?
- What are your opinions on the advice and support was given by the team with regards to these new difficulties?
- What or where would you seek for support or information if your care receiver's memory deteriorates further or does not improve?
- Describe risk assessment (Risk assessment is where health professionals use a number of factors that are unique to you in combination to guide deem whether you are high or low risk of a problem such as dementia. This enables them to tailor their advice, support and management to each individual). Are you aware of any risk assessment that currently takes place in clinical practice for dementia?

Views on Future Care

- What do you think might be the benefits in identifying stroke-survivors at risk of dementia earlier? Specifically:
    - For the patient
    - For their families
    - For doctors, nurses and the healthcare system
    - If not beneficial why not?
- Do you have any views on how healthcare professionals could identify those at risk of dementia?
- What do you think might be the benefits or barriers when involving the GP when memory difficulties do appear? Please elaborate - How could this be achieved?
- Can you think of any drawbacks in hospitals and GPs working together to manage this problem?

Views on Risk Assessment

- (Provide example of a risk assessment tool in dementia): What are your views in a risk assessment tool such as this to help identify stroke-survivors who are most at risk of dementia in the future?
- What are the benefits or problems associated with:
    - The delivery of the tool itself (by whom? where?)
    - The variables used in the tool
    - The outcome of the tool (high vs. low risk)

TOPIC GUIDE (1 YEAR POST-STROKE FIRST INTERVIEW)

Introduction and housekeeping

- Researcher to introduce an overview and the aim of the study. Need to reiterate their right to withdraw, pause the interview and confidentiality issues
- Seek permission to audio-record interview
- Ask whether they have any further questions
- Receive informed consent

Current Care Experience

- What is your experience of the care received by your family member/care receiver since their stroke?
- Can you tell me how your care receiver's memory has been?
- Have you needed to seek help for their memory difficulties at any point in the last 6 months
- Have you approached any health professional with their memory difficulties?
    - If yes – Who did you see? Why did you approach them? What are your opinions into the support/advice/management you were offered
    - If no – are there any reasons why you did not (any barriers to accessing healthcare services)?
- Has their memory affected your day to day living in the past 6 months
    - If so, how has it affected your day-to-day living and how have they managed this? How has it affected you as a carer?
    - If not, are there any reasons why this has been the case?
- Describe risk assessment (Risk assessment is where health professionals use a number of factors that are unique to you in combination to guide deem whether you are high or low risk of a problem such as dementia. This enables them to tailor their advice, support and management to each individual). Are you aware or has your care receiver been subject to any risk assessment that currently takes place in clinical practice for dementia? If yes – have you seen any benefits or problems with this approach?

Views on Future Care

- What do you think might be the benefits in identifying stroke-survivors at risk of dementia earlier? Specifically:
    - For the patient
    - For their families
    - For doctors, nurses and the healthcare system
    - If not beneficial why not?
- Do you have any views on how healthcare professionals could identify those at risk of dementia?
- What do you think might be the benefits or barriers when involving the GP when memory difficulties do appear? Please elaborate - How could this be achieved?
- Can you think of any drawbacks in hospitals and GPs working together to manage this problem?
- Having cared for someone living with memory difficulties following your stroke:
    - Are there in gaps in support/care that you feel are present which might be a barrier to better care?
    - Have you got any opinions on what could be put in place to better support you in the community?

Views on Risk Assessment

- Provide example of a risk assessment tool in dementia): What are your views in a risk assessment tool such as this to help identify stroke-survivors who are most at risk of dementia in the future?
- What are the benefits or problems associated with:
    - The delivery of the tool itself (by whom? where?)
    - The variables used in the tool
    - The outcome of the tool (high vs. low risk)

TOPIC GUIDE (1 YEAR POST-STROKE SECOND INTERVIEW)

Introduction and housekeeping

- Researcher to introduce an overview and the aim of the study. Need to reiterate their right to withdraw, pause the interview and confidentiality issues
- Seek permission to audio-record interview
- Ask whether they have any further questions
- Receive informed consent

Current Care Experience

- Can you tell me how your care receiver's memory has been since I last saw you?
- Have you needed to seek help for their memory difficulties at any point in the last 6 months? If yes please elaborate, if no what were the reasons behind this?
- Have you approached any health professional with regards to their memory difficulties?
    - If yes – Who did they see? Why did you approach them? What are your opinions into the support/advice/management they were offered
    - If no – are there any reasons why you did not (any barriers to accessing healthcare services)?
- Has their memory affected their day to day living in the past 6 months
    - If so, how has it affected their day-to-day living and how have they managed this? How has it affected you as a carer?
    - If not, are there any reasons why this has been the case?
- We talked about risk assessment at our last interview. As a reminder, risk assessment is where health professionals use a number of factors that are unique to you in combination to guide deem whether you are high or low risk of a problem such as dementia. This enables them to tailor their advice, support and management to each individual. Are you aware or has the care receiver been the subject of any risk assessment that currently takes place in clinical practice for dementia? If yes – have you seen any benefits or problems with this approach?

Views on Future Care

- Having cared for an individual with memory difficulties following their stroke:
    - Are there in gaps in support/care that you feel are present which might be a barrier to better care?
    - Have you got any opinions on what could be put in place to better support them in the community?
- Has your opinion changed as to whether you think we should be identifying stroke-survivors at risk of dementia earlier? Please elaborate

Views on Risk Assessment

- (Provide example of risk assessment tool in dementia): Last time we met we talked about whether a risk assessment tool would be clinically useful? What do you think about this now? Please elaborate

Appendix C: Co-Authorship Forms

Following advice I received from Professor Elaine McColl who had checked with Professor Tyson-Capper (email correspondence 8th June 2020), it was agreed that all senior (last author) and the corresponding author (if different) signatures should be obtained for the co-authorship forms. I am first author on all 7 publications presented in this thesis. In light of this, I have obtained the signatures as requested but also included the signatures of the other members of the supervisory team if they had been authors on the paper.

Newcastle University

SUBMISSION BY STAFF CANDIDATES FOR THE DEGREE OF PHD BY PUBLISHED WORK

CO-AUTHORSHIP FORM

This form must accompany any submission of a joint authored publication for the degree of Doctor of Philosophy on the basis of published work.

A candidate should submit a separate form for each jointly authored work which is submitted for the degree.

TITLE OF PUBLICATION (article, book, chapter, monograph)

Longitudinal Effect of Stroke on Cognition: A Systematic Review

DATE OF PUBLICATION 15th January 2018

NAME AND VOLUME OF JOURNAL (where appropriate)

Journal of the American Heart Association; (2018); Vol 7, Issue 2

PUBLISHER (for book, chapter or monograph)

N/A

EDITORS (chapter only)

N/A

ISBN (where appropriate)

N/A

If the work has not been published but has been accepted for publication please attach a statement from the Editor or Publisher which confirms the intention to publish the work.

NAMES OF JOINT AUTHORS	INSTITUTION
1. Obreniokibo Amiesimaka	Newcastle University
2. Stephanie Harrison	Newcastle University
3. Emma Green	University of Cambridge
4. Christopher Price	Newcastle University

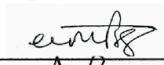
5. Louise Robinson (Newcastle University), 6. Mario Siervo (Newcastle University), 7. Blossom Stephan (University of Nottingham)

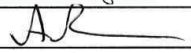
CONTRIBUTION OF THE CANDIDATE TO THIS WORK (%)

Design of investigation	60%
Conduct of research	50%
Analysis of outcome	75%
Preparation for publication	85%
TOTAL	67.5% *(To be an average of, or at least consistent with, the above figures)*

This statement should be endorsed by all of the co-authors.

I confirm that the above is a true estimate of the candidate's contribution to this work.

Signature 4 

Signature 5 

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TITLE OF PUBLICATION (article, book, chapter, monograph)

Impact of Memory Problems Post-Stroke on Patients and their Family Carers:

A Qualitative Study

DATE OF PUBLICATION 19th June 2020

NAME AND VOLUME OF JOURNAL (where appropriate)

Frontiers In Medicine; 7: 267

PUBLISHER (for book, chapter or monograph)

N/A

EDITORS (chapter only)

N/A

ISBN (where appropriate)

N/A

If the work has not been published but has been accepted for publication please attach a statement from the Editor or Publisher which confirms the intention to publish the work.

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1. Christoper Price	Newcastle University
2. Blossom Stephan	University of Nottingham
3. Louise Robinson	Newcastle University
4. Catherine Exley	Newcastle University

CONTRIBUTION OF THE CANDIDATE TO THIS WORK (%)

Design of investigation	80%
Conduct of research	85%
Analysis of outcome	75%
Preparation for publication	85%
TOTAL	81.25%

(To be an average of, or at least consistent with, the above figures)

This statement should be endorsed by all of the co-authors.

I confirm that the above is a true estimate of the candidate's contribution to this work.

Signature 1 _____

Signature 2 _____

Signature 3 _____

Signature 4 _____

Newcastle University

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TITLE OF PUBLICATION (article, book, chapter, monograph)

Gaps in care for patients with memory deficits after stroke: views of healthcare providers

DATE OF PUBLICATION 8th September 2017

NAME AND VOLUME OF JOURNAL (where appropriate)

BMC Health Services Research; 17, Article number: 634 (2017)

PUBLISHER (for book, chapter or monograph)

N/A

EDITORS (chapter only)

N/A

ISBN (where appropriate)

N/A

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TITLE OF PUBLICATION (article, book, chapter, monograph)

Post-stroke memory deficits and barriers to seeking help: views of patients and carers

DATE OF PUBLICATION 19th November 2018

NAME AND VOLUME OF JOURNAL (where appropriate)

Family Practice, Volume 36, Issue 4, August 2019, Pages 506–510

PUBLISHER (for book, chapter or monograph)

N/A

EDITORS (chapter only)

N/A

ISBN (where appropriate)

N/A

If the work has not been published but has been accepted for publication please attach a statement from the Editor or Publisher which confirms the intention to publish the work.

NAMES OF JOINT AUTHORS		INSTITUTION
1.	Christopher Price	Newcastle University
2.	Blossom Stephan	University of Nottingham
3.	Louise Robinson	Newcastle University
4.	Catherine Exley	Newcastle University

CONTRIBUTION OF THE CANDIDATE TO THIS WORK (%)

Design of investigation	80%	
Conduct of research	85%	
Analysis of outcome	75%	
Preparation for publication	85%	
TOTAL	81.25%	*(To be an average of, or at least consistent with, the above figures)*

This statement should be endorsed by all of the co-authors.

I confirm that the above is a true estimate of the candidate's contribution to this work.

Signature 1 _____

Signature 2 _____

Signature 3 _____

Signature 4 _____

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A candidate should submit a separate form for each jointly authored work which is submitted for the degree.

TITLE OF PUBLICATION (article, book, chapter, monograph)

Assessing the Predictive Validity of Simple Dementia Risk Models in Harmonized Stroke Cohorts

DATE OF PUBLICATION June 17th 2020

NAME AND VOLUME OF JOURNAL (where appropriate)

Stroke; Vol 51; Issue 7

PUBLISHER (for book, chapter or monograph)

N/A

EDITORS (chapter only)

N/A

ISBN (where appropriate)

N/A

If the work has not been published but has been accepted for publication please attach a statement from the Editor or Publisher which confirms the intention to publish the work.

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4. David Desmond	No Affiliation

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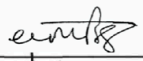
CONTRIBUTION OF THE CANDIDATE TO THIS WORK (%)

Design of investigation	77.5%	
Conduct of research	77.5%	
Analysis of outcome	83%	
Preparation for publication	70%	
TOTAL	77%	*(To be an average of, or at least consistent with, the above figures)*

This statement should be endorsed by all of the co-authors.

I confirm that the above is a true estimate of the candidate's contribution to this work.

Signature 1 

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Signature 3 

Signature 15 

Newcastle University

SUBMISSION BY STAFF CANDIDATES FOR THE DEGREE OF PHD BY PUBLISHED WORK

CO-AUTHORSHIP FORM

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A candidate should submit a separate form for each jointly authored work which is submitted for the degree.

TITLE OF PUBLICATION (article, book, chapter, monograph)

The views of public and clinician stakeholders on risk assessment tools for post-stroke dementia: a qualitative study

DATE OF PUBLICATION 27th March 2019.

NAME AND VOLUME OF JOURNAL (where appropriate)

BMJ Open 2019;9:e025586

PUBLISHER (for book, chapter or monograph)

N/A

EDITORS (chapter only)

N/A

ISBN (where appropriate)

N/A

If the work has not been published but has been accepted for publication please attach a statement from the Editor or Publisher which confirms the intention to publish the work.

NAMES OF JOINT AUTHORS	INSTITUTION
1. Catherine Exley	Newcastle University
2. Christopher Price	Newcastle University
3. Blossom Stephan	University of Nottingham
4. Louise Robinson	Newcastle University

CONTRIBUTION OF THE CANDIDATE TO THIS WORK (%)

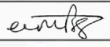
Design of investigation	80%
Conduct of research	85%
Analysis of outcome	75%
Preparation for publication	85
TOTAL	81.25%

(To be an average of, or at least consistent with, the above figures)

This statement should be endorsed by all of the co-authors.

I confirm that the above is a true estimate of the candidate's contribution to this work.

Signature 1 

Signature 2 

Signature 3 

Signature 4 

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SUBMISSION BY STAFF CANDIDATES FOR THE DEGREE OF PHD BY PUBLISHED WORK

CO-AUTHORSHIP FORM

This form must accompany any submission of a joint authored publication for the degree of Doctor of Philosophy on the basis of published work.

A candidate should submit a separate form for each jointly authored work which is submitted for the degree.

TITLE OF PUBLICATION (article, book, chapter, monograph)

Care Priorities for Stroke Patients Developing Cognitive Difficulties: A Delphi Survey of UK Professional Views

DATE OF PUBLICATION 5th August 2020

NAME AND VOLUME OF JOURNAL (where appropriate)

BMC Health Services Research; 20 (1); 717

PUBLISHER (for book, chapter or monograph)

N/A

EDITORS (chapter only)

N/A

ISBN (where appropriate)

N/A

If the work has not been published but has been accepted for publication please attach a statement from the Editor or Publisher which confirms the intention to publish the work.

NAMES OF JOINT AUTHORS	INSTITUTION
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2. Catherine Exley	Newcastle University
3. Darren Flynn	Teeside University
4. Blossom Stephan	University of Nottingham
5. Christopher Price	Newcastle University

CONTRIBUTION OF THE CANDIDATE TO THIS WORK (%)

Design of investigation 80%

Conduct of research 80%

Analysis of outcome 77.5%

Preparation for publication 80%

TOTAL 79% *(To be an average of, or at least consistent with, the above figures)*

This statement should be endorsed by all of the co-authors.

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